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CONTACT AND ENVIRONMENTAL ALLERGENS AS A CAUSE OF ECZEMA IN INFANTS AND IN CHILDREN

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There is general recognition of the important role played by contact and environmental allergens in the production of eczema in adults. Only during the past few years have advances been made in the study of these factors in eczema of infants and children. Because we have long been convinced of the importance of these factors in the etiology of eczema of infants and children, we feel that the results of our studies should be of value.

"CONGENITAL ALLERGY" IN CONTACT DERMATITIS

The literature still contains occasional references to "congenital allergy," as applied to contact dermatitis, notwithstanding the fact that most writers in recent years have expressed the opinion that one inherits not specific epidermal sensitivity but a predisposition or tendency to such sensitivity. A careful survey of the literature indicated that no observer had applied patch tests with common eczema-producing substances to a series of newborn infants. Straus [1] tested 119 newborn infants with extract of poison ivy with completely negative results. Adelsberger [2] did a great deal of work with infants, but few of her tests were on the newborn. There have been a few reports of patch tests in isolated instances of eczema in the newborn. No test gave a positive result.

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The material presented on congenital allergy is taken from work done by Dr. Walker at the Buffalo City Hospital in partial fulfilment of the requirements for the degree of Master of Science in Medicine, University of Buffalo School of Medicine.

1. Straus, H. W.: Artificial Sensitization of Infants to Poison Ivy, J. Allergy **2**:137-144 (March) 1931.

2. Adelsberger, L.: Das Verhalten der kindlichen Haut gegenüber verschiedenen Reizen, Ztschr. f. Kinderh. **43**:373-390 (May) 1927.

In our study 94 newborn white infants ranging in age from 2 to 8 days were used as test subjects. These newborn infants were all delivered in the same hospital and tested while remaining in the same nursery. Nine common eczema-producing substances, the ones used by Bloch,[3] were used in testing. In addition, a common toilet soap was included. The substances were as follows: mercury bichloride, 1 per cent aqueous solution; quinine hydrochloride, 1 per cent alcoholic solution; formaldehyde, 1 per cent aqueous solution; naphthalene, 1 per cent alcoholic solution; turpentine, 1 per cent alcoholic solution; tincture of arnica; iodoform; adhesive plaster; alcoholic extract of Primula abconica, and toilet soap, 1:100 dilution.

The test materials were applied to the back and removed at the end of twenty-four hours and the reactions noted. The sites were observed again at the end of forty-eight hours. In addition to these tests, an intradermal test to egg white, 1:25 dilution, was made of each infant and the result read at the end of thirty minutes. Every patch test in the entire series gave a negative result. Two infants 3 days old reacted to the intradermal test with egg white with wheal formation and true pseudopodia.

Time and space do not permit discussion of the significance of the 2 positive reactions to the intradermal injection of egg white. This phase of the problem has given rise to a voluminous literature. Suffice it to say that the weight of evidence and the generally accepted belief is that one of two things occurs: (1) Egg white antibodies may be carried directly into the fetal circulation from the mother (passive sensitization), or (2) egg white protein may gain entrance to the fetal circulation and the child's own tissues produce the specific antibodies (active sensitization). There is no evidence that a positive reaction to an intradermal test with egg white at birth is the forerunner of eczema.

Both infants with a positive reaction to egg white were reexamined two years later (table 1). Infant 1 gave a negative reaction to an intradermal test with egg white but a positive reaction to patch tests with mercury bichloride, quinine hydrochloride, formaldehyde and toilet soap. There had been no allergy in the family, but eighteen months after birth the child had impetigo and was treated with ammoniated mercury and the substance had been used extensively as a prophylactic for impetigo contagiosa shortly after birth. Examination of the child showed mild scaling of the left cheek and of the popliteal area of the right knee. Infant 2 had a negative reaction to an intradermal test with egg white. There was a history of hay fever in the mother and the brother, and

3. Bloch, B.: Role of Idiosyncrasy and Allergy in Dermatology, Arch. Dermat. & Syph. **19**:175-197 (Feb.) 1929.

the father had had hives. The child had had slight eczema about both ears two weeks after birth. Repetition of the patch tests gave negative results.

Of the remaining original group of 92 infants giving negative reactions to all tests, 71 were reexamined two years later. Four of these (table 1) had had eczema in varying degrees. These 4 infants were retested and a careful history taken. Three of the 4 had a positive reaction to a patch test with mercury bichloride. One of the 3 also reacted to formaldehyde and to toilet soap. Another gave a strongly positive papulofolliculopustular reaction to mercury bichloride, a mildly posi-

TABLE 1.—*Results of Patch and Intradermal Tests Made Two Years After Original Tests*

	Infant	
2 infants who had previously reacted to egg white	1	Impetigo at 18 months; ammoniated mercury prescribed; since then dermatitis of cheek and knee. No family history of allergy. Reaction to egg white negative; positive reactions to patch tests: mercury bichloride, ++; quinine, +; formaldehyde, ++; toilet soap, ++
	2	Mother and brother have had hay fever; father has hives. Patient had eczema of ears two weeks after birth; still present after two years. All patch tests and intradermal test gave negative results
4 infants who had had eczema	3	Family history irrelevant. Impetigo at age of 2 weeks; six weeks later eczema of scalp and forehead. At age of 19 months eczema of elbows after use of ammoniated mercury for inguinal adenitis. Reaction to patch test with mercury bichloride, ++; to all others negative
	4	Eczema of cheek at 2 months; cleared in six or eight weeks. Father had dermatitis venenata due to nickel. All tests gave negative results
	5	Three cases of eczema in mother's family. Eczema began on face at age of 2 months, spread to arms, legs, neck. Constant. Used no soaps and no feathers but wool sweater, coat and leggings. Reaction to egg white negative; to patch tests: mercury bichloride, ++; formaldehyde, +++; toilet soap, +
	6	Family history irrelevant. Eczema on cheeks at 2 or 3 months; remained 3 or 4 months; cleared under application of crude coal tar. Had previously used yellow salve (ammoniated mercury). Reaction to egg white, +++; to patch tests: mercury bichloride, ++++ (folliculopustular); toilet soap, +; primrose, +; adhesive tape, ++

tive reaction to toilet soap, to primrose and to adhesive tape and a positive reaction to the intradermal test with egg white. In the fourth case, all tests gave negative results, but the eczema was limited to one side of the face. In all 4 instances the history of onset, course and results of treatment and in 3 cases the results of the patch tests suggested ammoniated mercury ointment as the cause of the dermatitis. In the fourth case, in which the reaction to the patch test with mercury bichloride was negative, it must be remembered that the eczema was localized on the cheek and the patch test was applied to the back, under which circumstances one would not necessarily expect a positive reaction to the

patch test. Since observing these cases, we have been forced to conclude that the widespread use of 3 to 5 per cent ammoniated mercury in the prophylaxis of impetigo contagiosa in the newborn is a measure which although efficacious in preventing impetigo contagiosa may in many instances produce hypersensitivity in the skin of infants, thereby causing the child to be not only sensitive to mercurial preparations but more susceptible to other cutaneous sensitivities than other children.

As a result of our tests on newborn infants we can say definitely that there is no evidence that a child is born with any specific epidermal sensitivity. It is our belief that the child inherits predisposition to or ease of sensitization or, as Sulzberger [4] has expressed it, "a susceptibility to sensitization."

SCRATCH AND INTRADERMAL TESTS

Shortly after scratch tests were introduced, one of us (E. D. O.) had the opportunity, in 1920 and 1921, to supervise the performance of many hundreds of these tests. At the end of a year the tests were discarded as worthless as an aid in the etiologic study of eczema. It is true that few patients in this series were infants and not many more were children. Again, in 1923 and 1924, when intradermal tests had been introduced and popularized, one of us (E. D. O.), with the aid of a technician, performed from sixty to one hundred tests on a large series of patients, when a larger number of infants and children were studied. Conclusions, however, were the same as in the first series of scratch tests. Since that time, and usually coincident with the appearance of an article extolling the virtues of scratch and intracutaneous tests in the study of eczema, we have renewed our enthusiasm; but we have always obtained the same result. We have never been able to correlate the results of our tests or those of others with the actual clinical facts brought out by history and subsequent course. To rationalize scratch and intradermal tests to food proteins, one must assume that the ingested protein is absorbed at least partially unchanged and reaches the cutaneous cells in relatively the same form in which it exists in the material used for testing. Although this has been shown to be true of certain foods, particularly egg albumin, it demands a considerable stretch of the imagination to assume that this occurs in every instance in which a positive reaction to a scratch or an intradermal test exists. We are not deprecating the part that scratch and intradermal tests have played in scientific research and investigation into the fundamentals of allergy or the part that these tests play in the etiologic study of asthma and hay fever. It is significant that many dermatologists and allergists have recently called attention to the shortcomings of scratch,

4. Sulzberger, M. B.: Personal communications to the authors.

intradermal and patch tests. We refer particularly to the writings of Rowe,[5] Ramirez,[6] Rackemann,[7] Mendelsohn[8] and Sulzberger.[9]

PATCH TESTS

A great many of the criticisms leveled at scratch and intradermal tests apply to patch tests also, especially to patch tests of infants and children. In our opinion, patch tests of infants and very young children are of value only when two, three or four strongly suspected contact substances can be applied to an entirely normal area of skin adjacent to an eczematous area. In this way, clearcut reactions can sometimes be obtained. With infants it is frequently impossible to do a series of routine patch tests. The eczema is apt to be too generalized and the baby's skin too irritable to allow performance of satisfactory tests. Mild eczema may be made severe, and there is an added danger of inducing further hypersensitivity. Also, patch tests in general give negative results when the subject is atopic. These are all good and valid reasons for not doing routine patch tests on infants and young children. As will be emphasized later, we believe that patch tests are of more value in following up leads obtained by careful study of the history and of environmental and contact factors. Usually it is best to postpone patch tests until the acute stage of the eczema has subsided.

Peck and Salomon,[10] and Peck[11] deserve a great deal of credit for painstakingly performing patch tests on a series of 93 infants and children with twenty-one substances as well as performing sixty-two scratch tests in each case. They emphasized the importance of inhalants and contact substances as the cause of eczema and the value of the patch test in diagnosis. We agree with this conclusion, as well as with their statements regarding the lack of value of scratch tests and of

5. Rowe, A. H.: Evaluation of Skin Reactions in Food Sensitive Patients, J. Allergy **5**:135-147 (Jan.) 1934.

6. Ramirez, M. A., in discussion on Sulzberger, M. B.: Allergic Manifestations in Dermatology, New York State J. Med. **36**:1717-1723 (Nov. 15) 1936.

7. Rackemann, F. M.: History Taking in Allergic Diseases, J. A. M. A. **106**:976-979 (March 21) 1936.

8. Mendelsohn, H. V.: Sensitization Tests: Their Value in Dermatology, Arch. Dermat. & Syph. **29**:845-857 (June) 1934.

9. Sulzberger, M. B.: (*a*) Allergy in Dermatology: Critical Review of Some Recent Contributions, J. Allergy **8**:385-411 (May) 1937; (*b*) Suggestion for Classification of Certain Allergic Dermatoses, J. Michigan M. Soc. **34**: 78-84 (Feb.) 1935.

10. Peck, S. M., and Salomon, G.: Eczema of Infancy and Childhood: Contacts as Etiologic Agents, with Particular Reference to Feathers, Am. J. Dis. Child. **46**:1308-1328 (Dec.) 1933.

11. Peck, S. M.: Eczema of Infancy and Childhood; Neurodermatitis Disseminata (Type II Eczema); Atopy in Eczema, New York State J. Med. **34**: 957-964 (Nov. 15) 1934.

elimination diets. However, we believe that when the importance of inhalant and contact allergens has been once established there are more practical, less dangerous, more rapid and less costly methods of bringing about the desired result than by submitting infants and children with active eczema to a routine series of patch tests.

The efficacy of patch tests of infants and children with protein substances is a question of extreme importance in the investigation of this subject. It is the experience of practically all investigators that patch tests with protein substances, both in eczema of infants and children and in the atopic state, generally give negative results. Some authorities have gone even so far as to state that the reactions are always negative. That this is only part of the story is evident by the results of Peck and Salomon [10] and Peck,[11] who reported a relatively high percentage of positive reactions to patch tests with protein substances in eczema of infants and children. They reported 6 of 23 infants and 10 of 70 children from 2 to 12 years of age reacting to feathers. It is apparent that the field is fertile for further investigation, which may well reveal the crux of the relation of contact and environmental allergens to eczema of infants and to atopic dermatitis of children. We will summarize our views on this subject as follows, although our own observations are not of sufficient number, nor have we done enough experimental work, to justify definite conclusions: 1. We have seen sporadic positive reactions to patch tests with protein substances in both infants and children. These positive reactions have usually been delayed positive and have never been accompanied with vesiculation. 2. Frequently we have observed development of a patch of erythematosquamous eczema in an infant or a child at the exact site of friction from wool or feathers. Usually this original patch has been on the cheek, the neck, the elbow, the wrist or the popliteal space, and subsequently atopic dermatitis has developed on extensive areas as a result of dissemination of the offending allergen by the blood stream. 3. The ordinary patch test on the back or the arm of an infant or child does not approximate the actual clinical condition present in the production of a localized patch of eczema from contact with a protein substance. It is our impression that moisture and friction are necessary, and of course minute abrasion of the skin resulting from the friction. This statement is in line with the work of Hill,[12] who demonstrated that positive wheal reactions could be obtained to patch tests with proteins at points where the skin was rubbed with a tongue stick. We believe that this is the reason why in actual practice eczema due to a protein substance usually has its site of onset

12. Hill, L. W.: Sensitivity to Environmental Allergens in Infantile Eczema. New England J. Med. **213**:135-140 (July 25) 1935.

where the skin is thin, lacks a heavy, horny layer and is constantly exposed to friction and moisture. Before we can say that a patch test with a protein substance gives a negative result, we must follow the first rule of performing patch tests, namely: approximate the conditions actually present clinically. This is most easily done in practice by actual clinical trial, such as having the child wear a wool glove or a fuzzy wool sweater or coat. At present we are carrying on experiments to determine the efficacy of patch tests with protein substances on the flexor surfaces of the elbows and the knees.

Summarizing our impressions regarding patch tests with protein substances, we believe that the ordinary patch test on the back or the arm is of limited value. At present actual clinical trial is the only sure test.

Our interest in contact and environmental allergens as a cause of eczema in infants and children took definite form in 1927 and 1928. As stated previously, we were convinced at that time of the inadequacy of scratch and intradermal tests as a means of determining etiologic agents involved in a given case of eczema. We decided to hospitalize a series of infants and young children and to eliminate all contact and environmental allergens so far as possible. Our experiments in those years were undoubtedly imperfect, because we did not realize the importance of many minor factors. However, in two years 20 infants and young children were hospitalized and kept in cribs entirely surrounded by cotton garments, sheets, blankets and mattresses. For laundering only boiling was allowed. There were no contacts with wool, feathers, silk, oils, soap, pyrethrum, orris, kapok or other commonly known eczema-producing agents. Plain petrolatum, petrolatum with 0.5 per cent phenol or a simple lotion of equal parts of olive oil and solution of calcium hydroxide was applied. Restraint was used in some instances. Approximately 50 per cent of the patients were free of eczema in from four to eight weeks. All these children previously had received the usual dietary and local treatment, including application of crude coal tar. After leaving the hospital and returning to their home environments, most of these patients relapsed to their former condition. Since that time we have hospitalized many infants and young children with eczema, with the same percentage of good results. The attempt has always been made to eliminate contact and environmental allergens before further procedures are employed. In the carrying out of this program a searching detailed history is absolutely essential. The development of a high degree of skill as a detective is even more important and its application more highly specialized than in eczema in adults. Success or failure frequently hinges on a personal examination of every possible contact substance in the environment of the child. Immediate verbal answers by the parents or by nursemaids are notoriously unre-

liable, and experience has taught us that our results are in direct proportion to the time and effort expended in investigating the environment. The performance of patch tests with a standardized list of eczema-producing substances can never replace a careful, painstaking personal examination.

In handling eczema in infants and children, we have found procedure by the following steps the most effective:

1. Investigation of

(*a*) The family history of allergy. This is of slight importance in the individual case.

(*b*) A history of definite reactions to specific foods. This information is recorded for future use.

(*c*) The age at onset. We have never seen an infant under 10 days of age with eczema due to hypersensitivity.

(*d*) The exact location of the first area of eczema and the site of subsequent attacks, especially the first area to show evidences of exacerbation.

(*e*) Contact substances, including soaps, laundry chemicals, medicated oils, powders, wool, silk, feathers, dogs, cats, insect sprays, kapok, the mother's and father's cosmetics, hand lotions and toys.

(*f*) Previous treatment, especially by local applications.

2. Examination of the patient, with particular note of the area of onset, of sharply limited free areas, such as the nose, the upper lip and the chin and of sharp limitations at the ankles, the wrists and the cheeks. Evidence of dissemination of the offending allergen through the blood stream, and an estimate of the degree and extent of sensitization are extremely important.

3. Outline of treatment to the parents. This is often difficult, because many intelligent as well as ignorant parents refuse to believe in the importance of external contact and environmental allergens. It is essential to convince them that the first procedure is the elimination of these factors, which requires from four to eight weeks of observation. A list of the common contact and environmental allergens is given to them, with a detailed explanation that an infant must be kept in its crib or suspended in a canvas hammock and isolated from all contact and environmental allergens. We insist on the removal of all wool and silk from the room, including carpets, rugs and blankets, followed by frequent use of a vacuum cleaner. In cases of severe eczema we have insisted on hospitalization,[13] and in a number of instances the use of an air-conditioned room [14] has been of great assistance. However, in our experience the ordinary children's ward, free of all of the common contacts, has proved adequate for a fair trial with all except highly sensitized children. One of the main benefits of the air-conditioned room is the maintenance of an absolutely even temperature and humidity. As is well known, a high temperature frequently leads to excessive scratching, and when the humidity

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13. (*a*) Hill, L. W., and Sulzberger, M. B.: Evolution of Atopic Dermatitis, Arch. Dermat. & Syph. **32**:451-463 (Sept.) 1935. (*b*) Sulzberger, M. B.: Remarks on Definitions and Classification in Certain Forms of Dermatologic Allergy, New England J. Med. **215**:330-336 (Aug. 20) 1936.

14. Sulzberger, M. B., and Rostenberg, A., Jr.: Practical Procedures in Investigation of Certain Allergic Dermatoses, J. Allergy **6**:448-459 (July) 1935. Sulzberger.[9b]

is low the dryness of the skin tends to induce excoriation. We emphasize again that from four to eight weeks is essential for a proper test in many cases. Hospitalization for such a period is impossible for many families unless free ward beds are at the disposal of the physician. Our best results have come in cases in which such accommodations have been available. When one is once convinced of the importance of contact and environmental allergens in a given case, any subsequent exacerbation should be carefully investigated, preferably by personal inspection of the environment.

4. Subsequent office visits at one or two week intervals. Answers to well directed, searching questions relative to all common eczema-producing contact and environmental substances should be elicited.

5. Application of plain petrolatum, petrolatum with 0.5 per cent phenol or equal parts of olive oil and solution of calcium hydroxide. These are the only medicaments indicated during the test period.

6. Search for the specific cause of the eczema when the child is free of eruption. This can be done by patch tests, which are not always conclusive and, in our opinion, not as valuable as actual clinical trial.

7. Reexamination of the child and of the environment at the first sign of a recurrence.

8. Other methods of investigation, including elimination diets.

The aforementioned procedures are time consuming but more satisfactory than cutaneous tests and elimination diets in our opinion. Many parents will not cooperate, and the method demands infinite attention to detail on the part of the physician.

In going through our records, we found that since 1928 we have investigated 569 cases of eczema in infants and children from the standpoint of contact and environmental allergens. These were all observed in private practice, and at least as many more were observed in our clinics at the Buffalo City, the Buffalo General and the Children's Hospital. There is a special group of 24 patients whom we have followed for from five to twelve years. These patients have run the entire gamut of scratch and intradermal tests and elimination diets, and finally a careful search for environmental and contact allergens has been made, with a successful outcome.

In order to gain some definite statistical idea as to the efficacy of the latter method of approach, we have chosen patients whom we have seen since Jan. 1, 1935, for evaluation. From a total of 124 patients, 76 (table 2) had been followed sufficiently long to allow us to draw conclusions. Of 29 under 1 year of age, 6 were unimproved, 14 improved and 9 cured. Of 28 from 1 to 3 years of age, 2 were unimproved, 9 improved and 17 cured. Of 19 from 3 to 12 years of age, 3 were unimproved, 4 improved and 12 cured. It can be seen from these figures that of the entire group of 76 patients, 38, or exactly 50 per cent, were cured, 27, or 35 per cent, were improved and 11, or 15 per cent were unimproved. Our observations have led us to believe that

food atopens are frequently the etiologic factor in the last (unimproved) group and that multiple sensitivity to contact substances, inhalants, foods and possibly metabolic products are present in the middle (improved) group. In these groups our figures substantiate the impression that foods are of more importance in the etiology of eczema of infants than in that of children past 1 year of age. These figures confirm our experience of the past ten years, namely, that sensitization to contact and environmental allergens is the greatest single factor in the production of eczema of infants and children and that it is partially responsible, along with foods and other causes, in 35 per cent of the cases. In view of this, we believe that the first approach in the etiologic study of eczema in an infant or child is the elimination of contact and environmental allergens, unless other causes are obvious.

We are well aware that in many cases eczema in infants and children heals no matter what treatment is used. Application of crude coal tar has cured hundreds, as have the use of plain boric acid ointment and

TABLE 2.—*Statistical Survey of 76 Infants and Children Treated from Jan. 1, 1935 to Jan. 1, 1938*

Age	Number of Subjects	Cured	Improved	Unimproved
Under 1 year	29	9 (31%)	14 (48%)	6 (19%)
From 1 to 3 years	28	17 (60%)	9 (32%)	2 (7%)
From 3 to 12 years	19	12 (63%)	4 (21%)	3 (16%)
Totals	76	38 (50%)	27 (35%)	11 (15%)

roentgen irradiation. However, recurrence is the rule, and further investigation is almost always necessary. We are well aware that many patients lose their hypersensitivity spontaneously. We have seen this occur, as have other observers, after many forms of treatment and during the intercurrent infections, such as influenza, pneumonia, scarlet fever, malaria and osteomyelitis.

REPORT OF CASES

CASE 1.—The patient was a girl aged 3 years, whose mother and one maternal aunt had had eczema for more than ten years.

When she was 6 months old an eruption appeared in the cubital areas. This spread gradually until the face, ears, neck, forearms, wrists, buttocks and popliteal areas were involved. She received expert pediatric attention at a clinic for babies and two pediatricians in private practice. Scratch and intradermal tests had been performed, and the child had been on various diets for one year. The eczema had become steadily worse. There was no seasonal variation.

Examination showed an emaciated child of 3 years weighing 30 pounds (13.6 Kg.). Extensive erythematosquamous dermatitis was present on the ears, the neck, buttocks, thighs, hands, wrists and popliteal areas and to a lesser extent on the face.

Contact substances included wool, laundry chemicals and kapok. Treatment consisted of elimination of all eczema-producing contact substances and the application of a soothing calamine liniment. Two weeks later the child was 90 per cent improved. The itching had entirely disappeared. The mother then stated that the child had worn wool sweaters winter and summer. Three weeks later the child was entirely well except for slight lichenification.

She was then tested with wool protein and wool extract on the back, where no eczema had ever existed. The tests gave negative results but there was a general flare in the eczema, manifested by itching and subsequent scratch papules.

Two weeks later patches of wool protein and wool extract were applied to the flexor surfaces of the elbows and the knees (areas previously involved). Before one of the substances was applied the area was rubbed vigorously with a tongue blade. Within four hours the child began to itch generally but most markedly on the areas of old eczema. The mother noticed the child scratching all around the areas of the patch tests. The patches were removed at the end of forty-eight hours. Although there was an eczematous eruption all around the areas of the tests, at the exact area of testing there was no sign of eruption. The flexor surfaces of the knees and the elbows not covered by the patches showed a marked flare in the eczema.

This case illustrates the following points: (1) the inadequacy of scratch and intradermal tests and elimination diets so far as eczema of infants and children is concerned; (2) transepidermal absorption of the offending allergen through the normal skin with dissemination of the offending allergen through the blood stream and a generalized flare in the eczema, and (3) transepidermal absorption of the offending allergen and the production of a generalized flare. Even on the sites of preexisting eczema, patch tests gave negative results.

CASE 2.—In a boy, aged 6 years when seen, eczema had begun at the age of 4 months on the face, the neck and the flexor surfaces of the elbows. At the age of 9 months the eczema was generalized. Since that time the eczema had never entirely cleared, although there was some improvement in the summer. He had constantly been under the care of pediatricians, dermatologists and allergists. On two occasions he had had as many as a hundred scratch, intracutaneous and patch tests performed. He had had diets based on positive reactions to the tests, as well as Rowe elimination diets. Many forms of treatment had been used, including roentgen and ultraviolet irradiation, nonspecific desensitization with foreign proteins and all the usual forms of local treatment, among them application of crude coal tar, without beneficial results.

His mother had had dermatitis due to turpentine; an older brother had mild eczema, and a paternal aunt had hay fever.

Examination showed an undernourished anemic boy with a chronic lichenified dermatitis involving the flexor surfaces of the elbows, the right forearm, the back of the neck, the buttocks and to a slight extent the dorsa of the hands. A diagnosis of chronic atopic dermatitis was made.

A general well balanced diet was advised. This was given grudgingly by the mother and nurse for the first three months. All eczema-producing external contact substances and inhalants were removed from the boy's surroundings. These included soaps, laundry chemicals, feathers (he still had a feather pillow), kapok (he still used a kapok mattress), wool (clothing of all kinds, carpets, rugs and blankets) and cat hair. Four weeks later the skin was practically free of eruption. He inadvertently wore a wool coat and there was an immediate flare-up of the eczema in all areas. Six weeks later he was entirely free of

eczema, when suddenly a generalized erythema developed; this was followed by scaling. This was said to be due to eating oranges, although he had eaten many oranges since he was first seen. Careful investigation showed that he had again come in contact with wool. He remained entirely free of eczema for nine months and then had a sudden flare-up in all the old areas. His mother incriminated a feather pillow on which he had slept while away from home. Careful investigation showed that he had worn woolen mittens. There was no eruption, however, on the hands. He remained free of eczema for eleven months and then had a sudden flare-up in all the old areas. His mother blamed it on a feather pillow on which he had slept while visiting a friend. Investigation showed that he also used wool blankets. A subsequent test with woolen gloves on unbroken and noninflamed skin produced a prompt and marked flare in all the old areas of eczema.

This case illustrates the following points: (1) the inadequacy of cutaneous tests; (2) the impairment of general health over several years because of dietary measures which were unavailing; (3) the lack of careful investigation of environmental factors, and (4) transepidermal absorption as well as inhalation of the offending allergen.

CASE 3.—A girl aged 7 years was first seen in October 1928 because of dry papulosquamous eczema of the scalp and the neck. The diagnosis of seborrheic eczema was made, and under local treatment the condition disappeared in four weeks. She was next seen in October 1930, when she had mild eczema of the neck, the flexor surfaces of the elbows and the forearms. Under local treatment this condition was kept in check all winter, but no etiologic studies were made. The eruption cleared in the spring of 1931 and returned in the fall, continuing in the same manner until the fall of 1933, when a careful study was made. She had always been free of eruption except for occasional spots of eczema on her arms and neck when she was at the Atlantic seashore during the summer. As soon as she returned home in September the eczema recurred, gradually becoming more severe each year. In 1933 she reached puberty. Thorough scratch and intradermal tests were done, and elimination diets based on the results of these tests were instituted, with no benefit. The mother was then advised to remove all wool, silk, laundry chemicals and feathers. The eczema was improved for the remainder of the winter.

The girl was not seen for almost two years, but the condition during the intervening time continued in the fashion previously described. She had been entirely free all the summer of 1935 and when she entered her home in September she began to itch over the entire surface of the body. Eczema appeared on her face, neck, arms and trunk and behind the knees. All wool was removed from the patient's room, and when she was seen in April 1936, she stated that she had been better than for the previous two years. However, she still continued to wear wool. She tried living in another home for a month, but there was no change in the condition. During the summer of 1936 she was free of eruption and had a severe flare-up in September. This began one week before she left the seashore and coincided exactly with the onset of cool weather and her wearing of woolen sweaters and coats. The mother still insisted that the cause of the trouble was in the diet. Strenuous dietary measures were again tried with no result. The mother insisted then that the condition was caused by the dog, and the dog was taken away, with no benefit. The patient still continued to wear wool occasionally, and the eczema persisted. She was again free in the summer of 1937, and there was a prompt recurrence as soon as cold weather set in at

the seashore. This coincided with the wearing of woolen sweaters and coats. The eczema became progressively worse. The parents could not be convinced that it was due to wool. The patient was then placed in the hospital, away from all contact and inhalant allergens. The eczema cleared at least 95 per cent in two weeks.

Patch tests with over forty eczema-producing substances produced no positive results. However, the application of wool to the noninflamed skin produced a prompt and marked flare in the eczema. The application of wool protein to the normal skin produced a marked flare. Twice, in February and March 1938, the wearing of a wool coat produced a generalized itching within fifteen minutes. Her skin was comfortable when she could confine herself to a room in which wool in the air was minimal. Where wool carpets, blankets and rugs were present, generalized itching immediately developed. This case illustrates the following points: (1) marked hypersensitivity to wool; (2) transepidermal absorption of the offending allergen through normal skin; (3) uniformly negative reactions to patch tests in chronic atopic dermatitis; (4) inhalation of the offending allergen, and (5) the inadequacies of scratch, intradermal and patch tests in the study of chronic atopic dermatitis and hay fever.

There were asthma, hay fever and eczema on the father's side of the family. A brother, 5 years younger, had also had chronic atopic dermatitis of less severity, which was proved to be due to wool in the winter of 1936-1937.

TRANSEPIDERMAL ABSORPTION

Sulzberger [15] and Hill [12] have suggested the possibility of transepidermal absorption of water-soluble protein allergens in the production of chronic atopic dermatitis. Hopkins and Kesten [16] have expressed doubt of this phenomenon except in cases in which the skin is thin or has been traumatized. We are convinced that this phenomenon occurs not only at the site of localized eczema but through normal skin by dissemination of the offending allergen through the blood stream (case 1). We have demonstrated this repeatedly with a "glove test" (case 2); in some instances eczema of the hand and wrist with generalized symptoms was produced and in others no lesions developed at the site of contact but old areas of eczema immediately flared. After patch tests with protein allergens, including house dust, we have seen immediate generalized flares without any evidence of a positive reaction at the test site (case 3). Our observations have led us to conclude that water-soluble protein allergens are absorbed at any point of contact, moisture (especially perspiration) and friction being predominating factors. Inhalation is important only in highly sensitized subjects.

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15. Sulzberger, M. B.: Allergy in Dermatology: Discussion of Recent Contributions and of Their Relationship to Earlier Dermato-Immunologic Studies, J. Allergy **7**:385-427 (May) 1936; footnote 13*b*.

16. Hopkins, J. G., and Kesten, B. M.: Allergic Eczema: Eczema Initiated by Sensitization to Foods, Am. J. Dis. Child. **49**:1511-1530 (June) 1935.

CLASSIFICATION AND PATHOGENESIS

Time and space do not permit discussion of the classifications and pathogenesis of eczema in infants and children. Suffice it to say that we are, in general, in accord with the views of Sulzberger,[17] Hill [18] and others. All the available evidence points strongly to the facts that sensitivity to nonprotein allergens lies principally in the epidermis and that vesiculation is the primary clinical manifestation. The shock tissue in the case of water-soluble protein allergens is in the smaller blood vessels of the upper layer of the cutis; as a result of the inflammatory process itching occurs, and what one sees clinically is a secondary erythematosquamous dermatitis due to scratching. Our observations regarding transepidermal absorption tend strongly to confirm these views.

We can see no really essential difference between the eczema of infants and the eczema of older children. We believe the differences noted clinically can be explained by the differences in thickness and texture of the skin, in amount of moisture present, and in exposure to offending allergens. Both protein and nonprotein allergens gain entrance to the blood stream and produce generalized allergy of the epidermis or the blood vessels, as the case may be. In the case of nonprotein allergens, dissemination through the blood stream tends to produce a more or less generalized "id" eruption, whereas with water-soluble protein allergens the eruption tends first to be localized at points of friction and pressure, where rubbing against the clothes automatically scratches the skin. In this way, the flexor surfaces are the first to show evidences of dissemination of water-soluble protein allergens through the blood stream. Subsequently, all areas may partake in this reaction.

SUMMARY

Investigation of contact and environmental allergens in eczema of infants and children brings a high percentage of satisfactory results.

There is no experimental evidence that a person inherits any specific epidermal sensitivity. He does inherit an "ease of sensitization" or a "susceptibility to sensitization."

The widespread use of ammoniated mercury in the prophylaxis of impetigo contagiosa in the newborn is an important factor in producing eczema of infants and in widening the base of their allergy.

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17. Sulzberger, M. B.; Spain, W. C.; Sammis, F., and Shahon, H. I.: Studies in Hypersensitiveness in Certain Dermatoses: Neurodermatitis (Disseminated Type), J. Allergy **3**:423-437 (July) 1932. Sulzberger, footnotes 9*b* and 13*b*.

18. Hill, L. W.: Chronic Atopic Eczema (Neurodermatitis) in Childhood, J. A. M. A. **103**:1430-1434 (Nov. 10) 1934; footnote 12.

In our opinion, routine scratch and intradermal tests are entirely inadequate, unreliable and misleading in investigations of eczema of infants and children.

Routine patch tests of infants and children are not usually satisfactory. Actual clinical trial is more important. Patch tests with protein substances generally produce negative results in infants and children. As widely used, they do not conform to the first rule of patch testing, namely, that actual clinical conditions must be duplicated.

In an etiologic study of eczema of infants and children, we believe the first attack should be on the elimination of contact and environmental allergens. By this method we have succeeded in obtaining the following results: Fifty per cent were cured, 35 per cent were improved and 15 per cent were unimproved. In the "improved" group, we believe there were multiple sensitivities not only to contact and environmental allergens but to food atopens and possibly to metabolic products. From our experience, we do not believe that food atopens are of importance in more than 15 or 20 per cent of cases of eczema in infants and children.

We believe that transepidermal absorption of water-soluble protein allergens through both inflamed and noninflamed skin explains many of the clinical facts observed in patients sensitized to these allergens.

A careful, painstaking investigation of the history, a highly developed detective instinct and infinite attention to detail are more important than routine tests of any kind in determining the cause of eczema in infants and children.

MYCOLOGIC TECHNIC FOR THE STUDY OF ANASCOSPOROUS YEASTLIKE FUNGI

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It is not as yet possible to give a sharp systematic delimitation to the anascosporous yeasts. These are generally understood to be yeastlike fungi which have permanently lost their capacity to produce ascospores. It is not always easy, however, to determine when this has occurred.

Before studying any kind of yeastlike organism one has to be sure of the purity of the strain, for which Raulin's [1] solution is valuable. Several loopfuls of the culture are inoculated into this medium and incubated for three or four days at 37 C. or at room temperature, after which a loopful is taken from the Raulin solution and a pour plate made with 2 per cent dextrose agar. This is incubated at room temperature for two or three days, and an isolated colony is fished and streaked on a dextrose agar slant. The purity of the growth on the slant is later determined by direct examination of a thin suspension in double strength compound solution of iodine U. S. P. or of a specimen stained with Gram's solution.

When the pure culture is obtained, it is necessary to determine whether it is an ascosporous or an anascosporous yeast. The mediums that are most commonly used to demonstrate the production of sexual spores or ascospores are 2 per cent dextrose agar slants, carrot medium,[2] Gorodkova slants [3] and potato-carrot agar slants.[4] The growth on these

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1. Raulin, cited by Langeron, M.: Précis de microscopie, Paris, Masson & Cie, 1934, p. 1114.

2. For the carrot medium large carrots are selected, washed in hot water, scrubbed with a brush and peeled, and large cylindric pieces are removed with an apple corer. The cylinders are cut into wedges. The pieces are then inserted into the large variety of test tubes known as "potato tubes." In the bottom of each tube a small wad of absorbent cotton should be placed, with sufficient water to cover one-fourth the height of the carrot in the tube, in order to retard the drying of the carrot. The tubes are sterilized by fractional sterilization for from twenty minutes to half an hour in the Arnold sterilizer on three successive days.

3. For Gorodkova slants 10 Gm. of peptone, 10 Gm. of dextrose, 18 Gm. of agar and 1,000 cc. of water are required. The ingredients are dissolved in water, tubed and autoclaved for five minutes at 15 pounds' (6.8 Kg.) pressure. This

(Footnotes continued on next page)

mediums should be examined at definite intervals for the presence of ascospores by the following method:

A cover slip preparation of the organism in double strength compound solution of iodine is examined under a high dry lens for the presence of ascospores and for evidence of sexual conjugation. When the presence of ascospores is suspected, it may be verified by staining the preparation with Langeron and Guérra's [5] modification of Küfferath's spore stain. A thin saline emulsion of the organism is spread over a slide and dried over a flame. It is then stained for from three to five minutes with steaming Ziehl-Neelsen carbolfuchsin, decolorized in 2 per cent lactic acid in alcohol, washed in water and blotted gently. A small drop of dilute india ink is placed at one end of the slide and a thin smear of india ink is drawn over the slide in the way customary for drawing out blood films. The preparation is then dried, mounted and examined under oil. Spores stain red, and any conjugation will be visible. The india ink brings out the contour of the cells as they stand against a darkened background.

The macroscopic and microscopic morphologic characteristics of yeastlike fungi depend on the composition of the substrate on which they are grown, the age of the culture, the humidity of the medium and the temperature at which they were incubated. Giant colonies are best produced by inoculating the organisms onto a slant of 2 per cent dextrose agar with a stiff nichrome needle at two points about 2 cm. apart. The macroscopic aspect of a colony is extremely variable; therefore the gross appearance of giant colonies alone should not be taken as a dependable criterion in the identification of yeastlike fungi on any one medium. Sabouraud's "proof medium" is not satisfactory, since it is rich in sugar and, consequently, only a few yeastlike fungi are capable of producing filaments or any kind of spores on it. In order to obtain the maximum degree of filamentization and sporulation, the organism must be cultured on a "poor" medium, one containing only a small amount of sugar. Potato-carrot agar is excellent for this purpose. The microscopic structure of yeastlike fungi is best studied by the "slide culture" method originally described by Rivalier and Seydel [6] for the study of dermatophytes.

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medium contains only a small amount of sugar, which is rapidly exhausted by the fungus, after which the fungus begins to sporulate. Gorodkova slants must be fresh and have a moist surface in order to favor sporulation.

4. For potato-carrot agar slants potatoes and carrots are washed in hot water, scrubbed with a brush, peeled and then passed through a kitchen grater. Twenty grams of each vegetable is placed in a liter of tap water and boiled for from five to ten minutes. Solid particles are pressed through many layers of cheesecloth, and the juice expressed is mixed with the filtrate and the volume made up to a liter. Twenty grams of agar is then added. The mixture is melted and tubed in amounts of from 6 to 8 cc. in tubes 160 by 16 mm., autoclaved and slanted.

5. Guérra, cited by Langeron, M.: Précis de microscopie, Paris, Masson & Cie, 1934, p. 1131.

6. Rivalier, E., and Seydel, S.: Nouveau procédé de culture sur lames gélosées appliqué à l'étude microscopique des champignons des téignes, Ann. de parasitol. **10**:444-452, 1932.

"SLIDE CULTURE" TECHNIC

Three clean slides are put into a Borrel tube (fig. 1), one on each side of the prism, and sterilized in a dry air oven. The tube is then placed on a rack on its side, in such a way that its cover may be lifted without causing contamination of the contents with air bacteria and molds. A tubeful of potato-carrot agar medium is melted and spread in a thin layer on the surface of the slide by means of a thickly drawn-out Pasteur pipet bent at right angles. Sufficient time is allowed so that the medium may solidify on the surface of this first slide before the tube is rotated for smearing the other two slides. Each slide is then inoculated in two parallel lines about 1 cm. apart and about 7 mm. from the margin with a thinly drawn-out sterile capillary tube, the surface of which is charged with the culture. About 5 cc. of sterile water is then pipetted into the bottom of the tube to maintain optimum humidity. The tubes thus inoculated are then placed in a screw-capped jam bottle containing water 1 inch (2.5 cm.) deep.

Strains of yeastlike fungi which do not filamentize on this medium may be grown in an atmosphere of carbon dioxide put into the jam bottle from a Kipp generator. Although carbon dioxide favors filamentization, it will delay sporulation. Therefore, once filamentization has appeared, the carbon dioxide should be expelled, so that the conditions may be more favorable for sporulation. If a

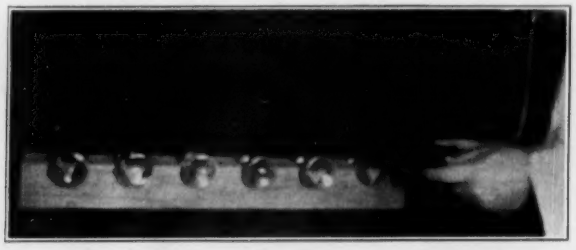

Fig. 1.—Apparatus for making slide cultures. Borrel tubes containing three slides, one on each side of the prism, are placed on a rack, and with a Pasteur pipet the medium is spread as a thin film on the surface of each slide.

yeastlike fungus does not filamentize on potato-carrot agar in the presence of carbon dioxide on repeated trials, it may be rightly considered to belong to the group of fungi commonly known as torulae. The slides showing adequate filamentization and sporulation are removed from the tubes, throughly dried in an incubator (two or three days at 37 C.), fixed for from three to five minutes in 95 per cent alcohol and stained for from five to fifteen minutes with acetic-cotton blue.[7] The dye is poured off, and the slide is rapidly washed in water and passed through graded alcohols and then through two changes of xylene and mounted in euparol. The slide culture technic gives excellent permanent preparations in which the microscopic structure of the fungus is clearly visible and the relation of various types of spores to the mycelium remains intact (fig. 2).

It is important to know whether a yeastlike fungus is capable of forming mycelium. If it is, it is then necessary to distinguish between true mycelium and pseudomycelium. True mycelium is either a non-

7. For acetic-cotton blue 100 cc. of distilled water, 1 cc. of cotton blue C4B Poirrier and 3 cc. of glacial acetic acid are mixed, dissolved in a mortar and filtered before use.

septate filament which may eventually give branches or a septate branching filament in which the septums are produced as transverse ingrowths from the wall of the hypha. Pseudomycelium may be septate and branched; yet it differs from true mycelium in that the septums, instead of being ingrowths from the wall of the filament, are produced as the result of successive terminal or lateral budding processes. The hyphal cells in the pseudomycelium arise by budding. The buds may be terminal, subterminal or lateral and single or multiple and may appear simultaneously or in succession. These processes may be studied by the aforementioned slide culture method or by liquid culture in some such medium as potato water [8] or malt water, from which a loopful of a

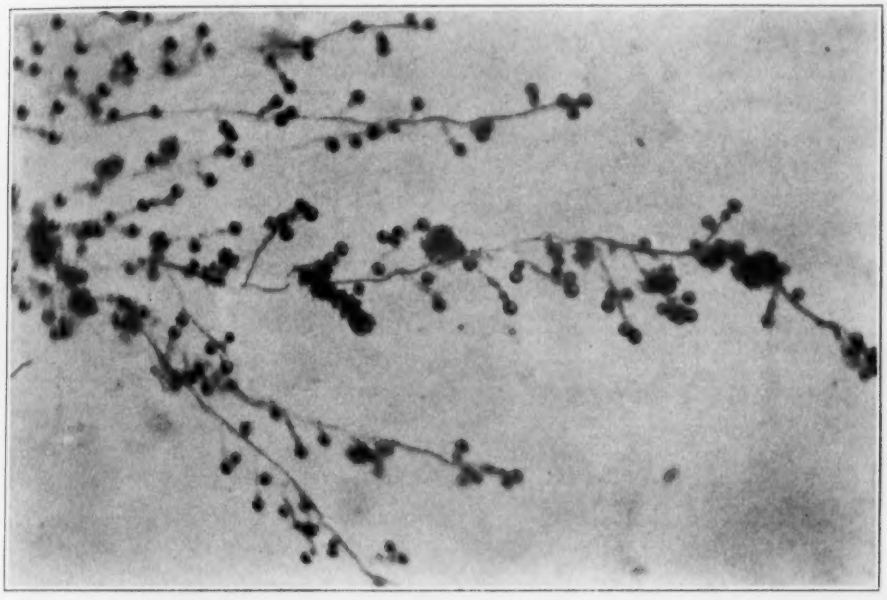

Fig. 2.—Filamentization and sporulation of Monilia albicans. Blastospores and terminal and lateral chlamydospores are evident (photographed from a "slide culture").

culture several days old is mixed with a drop of double strength compound solution of iodine and examined under the microscope.

Measurements of fixed and stained samples of yeastlike fungi are not of much significance in the identification of species, except for those yeastlike fungi which are strictly unicellular and occur as round or oval cells with no tendency to elongate.

8. For Langeron's potato water medium a potato is peeled and the pulp grated. Twenty grams of the substance is soaked in a liter of water, allowed to macerate for an hour and then boiled gently for about five minutes. The mass is filtered through cotton, tubed and autoclaved at 15 pounds' (6.8 Kg.) pressure for fifteen minutes.

BIOCHEMICAL STUDIES

The biochemical reactions of yeastlike fungi are often of great value in the identification and differentiation of members of this group. The capacity of the fungus for liquefaction of gelatin, for fermentation of sugars, for assimilation of carbohydrates and of nitrogenous substances and for production of carotenoid pigment will be considered under this heading.

Liquefaction of Gelatin.—The test for liquefaction of gelatin has been borrowed from bacteriology. Although Stelling Dekker [9] and Lodder [10] have used the test extensively as a differential procedure, the method is unsatisfactory, because the results vary with different batches of gelatin. Frequently the liquefaction is slight and may take from forty to eighty days to appear.

Fermentation of Carbohydrates.—Unless one is working with a pure strain of fungus, free from bacterial and other contaminants, tests of fermentation are a waste of time and material, as the results obtained will be neither reliable nor constant. Castellani [11] used seventeen or more different carbohydrates in the identification of yeastlike fungi. Additional information of differential value cannot be gained merely by multiplying indefinitely the number of carbohydrates used. The first step is to determine whether the fungus under study can ferment dextrose with the production of acid and gas. Without known exception, if a yeastlike fungus does not ferment dextrose, it does not ferment any other carbohydrate. If dextrose is fermented, the carbohydrates which may be used to gain additional valuable information are lactose, maltose, levulose, saccharose, galactose and raffinose. Attempts at a finer differentiation by the determination of degree of production of acid with suitable indicators are not only unnecessary but may be sources of avoidable confusion, as a yeastlike fungus may produce a reaction at first acid, later alkaline and finally acid again. It may produce acid aerobically, anaerobically or both. It may produce acid or gas early or late.

Reactions of fermentation so far as the production of gas is concerned are fairly constant and, no doubt, of value in the identification of yeastlike fungi; but their study must not be made in a haphazard way if uniformity of results is anticipated. The preferable method for studying reactions of fermentation is that practiced by Guérra: [12]

9. Stelling Dekker, N. M.: Die Sporogenen Hefen, Amsterdam, Drukkerij, 1931.

10. Lodder, J.: Die Anaskosporogenen Hefen, Amsterdam, N. V. Noord-Hollandsche Uitgeversmaatschappij, 1934.

11. Castellani, A.: The Plurality of Species of the So-Called Thrush Fungus (Champignon du muguet), Ann. Inst. Pasteur **30**:149-154, 1916.

12. Guérra, P.: Role des levures en dermatologie (étude clinique et mycologique), Paris, Vigot Frères, 1935.

A 2 per cent solution of the carbohydrate is prepared in 1 per cent peptone water and tubed in 4 cc. amounts in bacteriologic culture tubes of good quality (120 by 12 mm.). A sterile mixture of 2 parts of hard paraffin and 1 part of petrolatum is then melted and pipetted into the tubes in amounts sufficient to cover the surface of the solution with a layer from 3 to 5 mm. thick. The tubes are sterilized fractionally and incubated for forty-eight hours to insure sterility. Just before use the paraffin on the surface is melted by holding the middle of the tube over the pilot flame of a Bunsen burner, and the solution of sugar is then inoculated in the usual way. The tube is immediately placed in a vertical position, to allow the paraffin to harden on the surface in uniform thickness. The tubes are then placed in the incubator at from 25 to 30 C. and observed at regular intervals for a fortnight for the production of gas.

Assimilation of Carbohydrates.—The auxanographic method of Beijerinck [13] is of considerable value in the study of yeastlike fungi. A yeastlike fungus may not be capable of fermenting a particular carbohydrate and yet be able to grow in its presence. In order to be certain that the growth of the fungus is directly dependent on the presence of a particular substrate, one must exclude all other available sources of nutrition. I recommend the following medium for this purpose, which I call basic medium:

	Gm. or Cc.
Potassium dihydrogen phosphate	1.00
Magnesium sulfate	0.50
Agar agar	20.00
Distilled water	1,000.00

This medium can be prepared and tubed in the form of "deeps" or "longs" and used whenever needed. It should be noted that, even in the total absence of available nitrogen in the medium, the addition of a suitable carbohydrate will stimulate growth and multiplication; probably nitrogen is derived from the dead cells, which are numerous in the heavy inoculum.

Technic: A homogeneous emulsion of a young culture of the yeastlike fungus under study is made, and 1 or 2 cc. is put into a Petri dish. A "deep" of the basic medium, melted and cooled to about 45 C., is poured over this. The agar is thoroughly mixed with the suspension of the fungus and allowed to harden. One or two centigrams of each carbohydrate is then placed at each of four diametrically opposite points on the surface of the agar. A strip of sterile filter paper is then passed between the cover and the bottom plate of the Petri dish to absorb the water of condensation, and the plate is incubated upside down at from 25 to 30 C. for forty-eight hours. By holding the plate before a good source of light, the relative degrees of growth in the zones of the several carbohydrates (fig. 3, upper circle) may be determined. As a warning against possible errors in the reading of results of tests for assimilation, the following observations may be useful: 1. If a fungus

13. Beijerinck, M. W.: Versl. d. k. Akad. v. Wetensch. **6**:123, 1889; cited by Lodder,[10] p. 60.

does not assimilate dextrose, it does not assimilate any other carbohydrate. 2. If a fungus is capable of assimilating dextrose, it almost invariably assimilates levulose and often mannose. 3. If a yeastlike fungus assimilates lactose, it is usually unable to assimilate maltose, and vice versa.

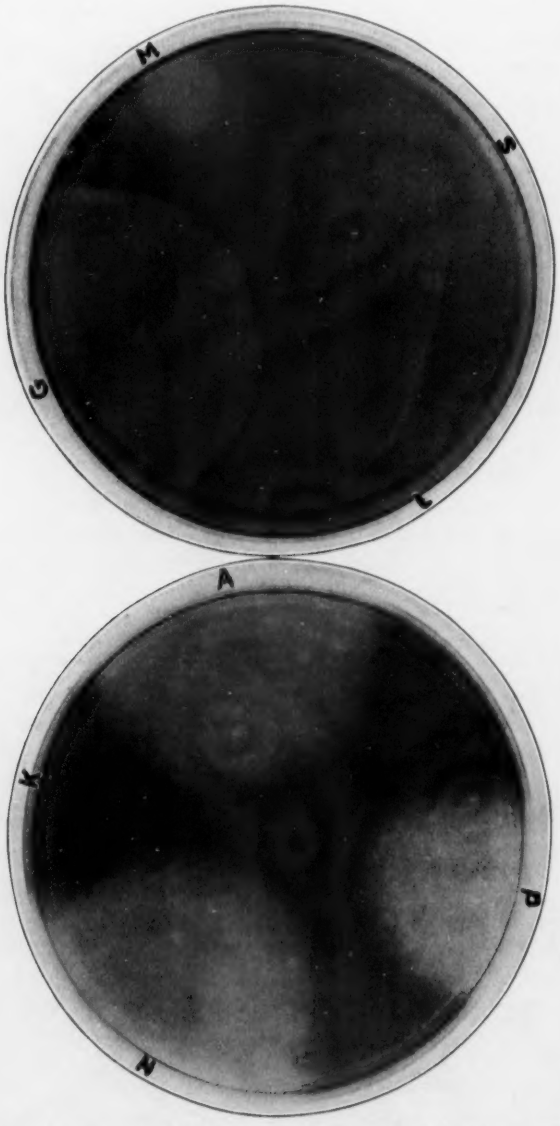

Fig. 3.—Upper circle, assimilation of carbohydrates by M. albicans. *G* (dextrose), *S* (saccharose) and *M* (maltose) are assimilated; *L* (lactose) is not assimilated. Lower circle, assimilation of nitrogenous substances by M. albicans. *P* (peptone), *A* (asparagine) and *N* (ammonium sulfate) are assimilated; *K* (potassium nitrate) is not assimilated.

After having worked with a large number of carbohydrates, I have found dextrose, lactose, maltose, saccharose and galactose of value in differentiation and identification of yeastlike fungi.

Assimilation of Nitrogenous Substances.—The assimilation of nitrogenous substances is often of greater significance than that of the carbohydrates. The test is essentially the same as that for the assimilation of carbohydrates, except that a different medium is used. The medium for the assimilation of nitrogenous substances is made by adding 20 Gm. of dextrose to the formula given previously for the basic medium. Although most yeastlike fungi grow slightly on this medium alone, the growth is greatly enhanced in the presence of a suitable nitrogenous substance, such as potassium nitrate, ammonium sulfate, urea, peptone, asparagine, histidine and tryptophan. If a yeastlike fungus does not assimilate peptone it will not assimilate any other nitrogenous substance, and almost invariably yeastlike fungi assimilate peptone with more or less avidity (fig. 3, lower circle).

Production of Carotenoid Pigment.—The usual method for determining the presence of carotenoid pigment is that of Molisch:[14]

> The fungus under study is grown on 2 per cent dextrose agar in large test tubes or in Blake bottles. The growth is washed and centrifuged. To a few grams of the sedimented cells 2 cc. of 20 per cent solution of potassium hydroxide in 40 per cent alcohol is added. The tube is kept in the dark for twenty-four hours. Then a small quantity of the sediment is placed on a slide with a Pasteur pipet and examined under the microscope for the presence of red or orange-red crystals of carotenoid pigment.

Lodder[10] recommended this method, but I have not found it satisfactory.

SEROLOGIC STUDIES

Recently a number of papers emphasizing the value of serologic methods in the differentiation of the so-called monilias have appeared. Benham[15] correlated the morphologic classification with that obtained by observing the absorption of agglutinins and recommended study of direct agglutination as an aid in the recognition of the species of monilia. Stone and Garrod[16] made use of the complement fixation and the precipitation reaction in the identification of yeastlike fungi and claimed that all organisms isolated from thrush fall into one group

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14. Molisch, H.: Mikrochemie der Pflanze, Jena, 1921, p. 250; cited by Lodder,[10] p. 36.

15. Benham, R. W.: Certain Monilias Parasitic on Man, J. Infect. Dis. **49**: 182-215, 1931; Monilias, Yeasts and Cryptococci: Their Pathogenicity, Classification and Identification, Am. J. Pub. Health **22**:502-504, 1932.

16. Stone, K., and Garrod, I. P.: Classification of Monilias by Serological Methods, J. Path. & Bact. **34**:429-436, 1931.

corresponding to Monilia albicans. They reported that their immune serums gave positive precipitation and complement fixation reactions to six different species of monilias described by Castellani. M. tropicalis, though giving positive precipitation and complement fixation reaction to the antiserum of M. albicans, is a distinct species readily identifiable on morphologic and biochemical grounds.

Serologic criteria alone should not be depended on in the identification of yeastlike fungi until more extensive work has been done on the antigenic constitution and relationships within this group of fungi. At present the immunologic reactions of this group of organisms are of value only as an adjunct to morphologic and biochemical studies.

SUMMARY

A method for the study of anascosporous filamenting yeastlike fungi is described. The method consists of (1) purification of mixed cultures by the use of Raulin's liquid; (2) determination of production of sexual spores or ascospores by growing the fungi on carrot medium, on Gorodkova's medium, on potato-carrot agar medium and on 2 per cent dextrose agar medium; (3) the use of a differential spore-staining technic, which is described; (4) morphologic studies of giant colonies of microscopic structure by means of a "slide culture" technic and of growth of the organism on potato water medium; (5) studies of appropriate biochemical reactions, such as liquefaction of gelatin, fermentation of carbohydrates, assimilation of carbohydrates and of nitrogenous substances and production of carotenoid pigment.

The serologic methods hitherto used in the study of yeastlike fungi are briefly discussed.

LIQUEFYING NODULAR PANNICULITIS

REPORT OF A CASE

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Circumscribed or nodular inflammatory diseases of the subcutaneous fatty tissue have not been the subject of a great deal of study, as this tissue is seldom the primary site of a disease process. Most frequently the involvement is secondary to an incidental or adjacent pathologic focus. However, a number of distinct clinical entities in which the subcutaneous fatty tissue apparently plays the fundamental or characteristic role have recently been receiving a greater degree of recognition.

Most of these entities can be grouped under the generic term subcutaneous fat necrosis,[1] although many other terms indicative of the same process are found in the literature, such as cystosteatonecrosis,[2] lipogranuloma,[3] lipogranulomatosis,[4] lipodystrophy[5] and liponecrosis.[6] The process is essentially granuloma of the fatty tissue in which the fat undergoes lysis and subsequent phagocytosis and in which characteristic foam cells and giant cells of foreign body type are present.

Clinically, the picture is marked by the formation of one or more subcutaneous, nontender, indolent and woody nodular masses, which usually undergo spontaneous involution after several months or years.

From the Department of Dermatology and Syphilology of the School of Medicine, University of Pennsylvania, John H. Stokes, M.D., Director.

1. Shoug, G., and Cowan, A.: Subcutaneous Fat Necrosis of the Newborn, Ohio State M. J. **34**:34-35, 1935. Mosto, D.: Contribution al estudio de la cistoesteatonecrosis subcutanea, Prensa méd argent. **18**:414-426 and 452-571, 1931.

2. Bindschedler, J. J., and Euguy: Un cas de cystostéatonécrose du nouveau-né, Bull. Soc. de pédiat. de Paris **34**:391-394, 1936. Gaviolo, R. L., and Rodriquez, J. M.: Cistoesteatonecrosis subcutanea, Semana méd. **1**:527-532, 1936.

3. Cracium, E. C.: Sur le tissu hémato-conjonctif, Bull. Acad. de méd. de Roumanie **1**:203-206, 1936.

4. (*a*) Chlapobersky, V.: La lipogranulomatose (necrose graisseuse, granulomes graisseuse) et son importance dans la clinique chirurgicale, Rev. de chir., Paris **53**:287-327, 1934. (*b*) Goldzieher, M. H.: Lipogranulomatosis (Makai), Arch. Surg **23**:690-702 (Oct.) 1931.

5. Rowe, A. H., and Garrison, O. H.: Lipodystrophy: Atrophy and Tumefaction of Subcutaneous Tissue Due to Insulin Injections, J. A. M. A. **99**:16-18 (July 2) 1932.

6. Morone, G.: Sulla liponecrosi sottocutanea multipla, Clin. chir. **32**:25-84, 1929.

The most common exciting cause of this condition is trauma to the subcutaneous fatty tissue. The disease appears most frequently in newborn infants and in women's breasts, in incisional scars and at the sites of subcutaneous injections of various foreign substances, especially mineral, vegetable and animal oils. Rarely these lesions may appear after acute febrile diseases.[4a] Sometimes no etiologic factor can be found. Excellent reviews of the subject have recently been made by Chlapobersky [4a] and Goldzieher,[4b] and illuminating pathologic and experimental investigations have been reported by Cracium,[3] Neal and Ellis [7] and Woringer.[8]

Under the title relapsing nonsuppurative nodular panniculitis Weber [9] described a case of a clinical syndrome characterized by recurrent crops of subcutaneous nodules and accompanied with febrile episodes. Subsequently Christian [10] reported a number of additional cases under the modified title relapsing febrile nonsuppurative nodular panniculitis. Later reports by Alderson and Way [11] and Bailey [12] have added to the knowledge of the disease. Bailey reported that the characteristic features of the disease are

> (1) recurrent attacks of malaise and fever, of widely varying degree, accompanied by subcutaneous nodules; (2) predominant occurrence of the condition in adult women; (3) localization of the subcutaneous nodules on the trunk or extremities but mainly on the thighs, and (4) a tendency to subcutaneous atrophy with its resultant depression at the site on involution. The histologic features are (1) edema and necrosis, primarily involving the subcutaneous fat; (2) diffuse appearance of cells phagocytic for fat, with a few multinucleated cells; (3) very limited fibroblastic stimulation; (4) notable absence of epithelioid nodules; (5) infrequent, severe vascular changes, and (6) primary involvement of the entire fat lobule.

Bailey stated that, although the cause of the disease is not known, it probably represents a particular type of reticuloendothelial response to some etiologic factor or factors. He stressed, especially, the possible role of drugs, particularly bromides and iodides.

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7. Neal, M. P., and Ellis, M. M.: Experimental Fat Necrosis in Various Vertebrates, Am. J. Clin. Path. **1**:251-263, 1931.

8. Woringer, F.: Contribution à l'histopathologie du tissu adipeux, Ann. de dermat. et syph. **2**:1089-1103, 1931.

9. Weber, F. P.: A Case of Relapsing Non-Suppurative Nodular Panniculitis Showing Phagocytosis of Subcutaneous Fat-Cells by Macrophages, Brit. J. Dermat. **27**:301-311, 1925.

10. Christian, H. A.: Relapsing Febrile Nodular Nonsuppurative Panniculitis, Arch. Int. Med. **42**:338-351 (Sept.) 1928.

11. Alderson, H. E., and Way, S. C.: Relapsing Febrile Nonsuppurative Panniculitis (Weber), Arch. Dermat. & Syph. **27**:440-449 (March) 1933.

12. Bailey, R. J.: Relapsing Febrile Nodular Nonsuppurative Panniculitis (Weber-Christian Disease), J. A. M. A. **109**:1419-1425 (Oct. 30) 1937.

I shall report a case of nodules in the subcutaneous fatty tissue, associated with fever. In this case, however, the nodules underwent liquefaction and subsequently ruptured with the discharge of an oily or fatty liquid. So far as can be found from a perusal of the literature, no such syndrome has ever been described.

This case was presented by Shaffer and Pillsbury [13] at the Atlantic Dermatologic Conference on Dec. 11, 1937. No diagnosis was offered by the members at the session.

REPORT OF CASE

E. K., a white woman aged 33, a hosiery worker, born in Philadelphia of Irish parentage, was admitted to the Hospital of the University of Pennsylvania on Nov. 12, 1936.

The family history was not significant. The patient's father had died at the age of 47 of an unknown condition. Her mother was living and in good health at 65 years. Four siblings, aged 39, 37, 29 and 21, were well; several others had died in infancy. There was no history of tuberculosis, syphilis, pyogenic infection, endocrine disorders, allergic disease, nephritis, hypertension or cancer.

The past medical history was not important. The patient recalled no diseases of childhood. At the age of 10 or 12 years she had suffered from pneumonia. She had had no other illnesses.

Her current trouble began in 1926, when over a period of months a number of "abscesses" developed. These terminated after tonsillectomy. In March 1936 an infection developed on the dorsum of the left foot; this was treated and apparently "cured" in two weeks.

Two months later she was admitted to the Northeastern Hospital because of multiple "abscesses," located chiefly on the thighs and buttocks. An occasional lesion was present on the arms. No history of ingestion of drugs could be obtained. The patient remained in the hospital for four and one-half months and was then discharged as cured (September 1936). Cure was attributed to a course of intravenously administered typhoid vaccine. Also, several suspicious teeth had been extracted. During her stay at this institution she was studied extensively. Many urinalyses gave normal results. Repeated blood counts showed nothing significant except slight leukopenia (from 4,000 to 5,500 leukocytes). Several cultures each of the blood, of fluid from the "abscesses" and of the urine were negative. The phenolphthalein test showed normal renal function. The cholesterol content of the blood varied from 110 to 135 mg. per hundred cubic centimeters; the urea nitrogen content was 11 mg. and the sugar content 85 mg. per hundred cubic centimeters. The basal metabolic rate was —11 and —9 per cent on two occasions. Serologic tests of the blood for syphilis were negative. Roentgen examinations of the sinuses, the pelvis, the sacrum and the spinal column revealed no abnormalities. A flat roentgenogram of the abdomen showed a moderately enlarged spleen, associated with a slight downward displacement of the left colic flexure.

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13. Shaffer, B., and Pillsbury, D. M.: A Case for Diagnosis (Recurrent Furunculoid Lesions of the Adipose Tissue), Arch. Dermat. & Syph. **38**:153 (July) 1938.

Within a few weeks of her discharge from the Northeastern Hospital the lesions recurred, and the disease progressed with increasing severity until the time of her admission to the Hospital of the University of Pennsylvania, in November 1936.

At that time the patient was described as a cooperative, intelligent, somewhat emaciated woman of about 25 years (appearing much younger than her stated age of 33). She seemed moderately febrile but rather more uncomfortable than acutely ill. Because much pain was associated with any active or passive movement that caused pressure on the numerous lesions, the patient held herself rigidly in bed, which rendered examination rather difficult. Except for these lesions, the general physical examination showed only a barely palpable nontender spleen. The mucous membranes were normal. There was no adenopathy.

The lesions were found to be restricted to the buttocks and extremities but were disposed most numerously on the buttocks, thighs and calves and the external aspect of the arms. There were from twenty to twenty-five active lesions in all stages of development, together with an equal number of scars marking the sites of previous lesions. Several incisional scars were also found, where the "abscesses" had been surgically opened.

The active lesions varied in size. The earliest were detected only by palpation, as woody, tender and painful masses varying in size from that of a walnut to that of an egg and lying deep in the subcutaneous tissue. There were no changes in the appearance of the skin over these lesions. Later lesions had increased to the size of an apple, raising the skin over them in the shape of an erythematous or violaceous mound. Many of these lesions were found to be fluctuant, and in the oldest of them a bulla-like covering of translucent violaceous skin was spread over the yellowish fatty fluid contents of the lesion. In several instances the attenuated skin had ruptured, and an oily yellowish or brownish fluid full of fat globules was being discharged.

During the patient's stay in the hospital the development and course of the lesions was closely followed. It was noted that new lesions appeared in crops of three or four, beginning as deep-seated, painful and tender infiltrations which in two or three days involved the overlying skin, causing it to become elevated and red and still later to assume a violaceous hue. When the lesion was 5 or 6 days old it became fluctuant. At the end of from seven to ten days the typical lesion had grown from the size of a walnut to that of a fist and had the appearance of a cyanotic or violaceous tumor partially elevated above the general cutaneous surface. The center of this mass was raised in the form of a translucent membrane, through which the yellowish fluid contents of the mass could be discerned. This window-like covering rapidly ruptured, and large quantities of a yellowish or yellowish brown liquid were discharged. Often as much as 3 or 4 ounces (from 90 to 120 cc.) of fluid was collected from a single lesion. With rupture and discharge, the pain soon subsided, and the lesion underwent rapid involution. The interval between the time at which the patient first experienced deep pain and tenderness and the time when the lesion ruptured was usually from ten to fourteen days. The discharge continued, as a rule, for four or five days, and finally the lesion healed, in two or three weeks. Eventually there remained at the site only a deep-seated, slightly puckered scar, set in a cup-shaped depression of the adipose tissue. Many of these scars became pigmented.

The patient remained under my observation until the writing of this report (February 1938). She remained in the Hospital of the University of Pennsylvania until March 4, 1937, and subsequently was studied by me in the

dermatologic outpatient department. During her first month in the hospital the temperature ranged almost constantly from 101 to 103 F. (38.4 to 39.6 C.), but during the second and third months of treatment (described later in the report) the fever became intermittent, and the temperature almost never rose above 100 F. (38 C.). Since that time, except for a few minor fluctuations, the temperature has remained normal.

Generally the appearance and development of the lesions followed the course of the fever; yet after the temperature became normal and remained so new lesions continued to appear, although in much scantier numbers. In the last few months of observation (December 1937 to February 1938) only a few abortive and superficial lesions occurred, and none appeared during the last six weeks. The total period of observation of this patient was fifteen months.

Fig. 1.—Photograph of patient on Nov. 15, 1937, showing several small active lesions. Numerous pigmented and nonpigmented scars set in cup-shaped depressions can be seen.

While the patient was in the Hospital of the University of Pennsylvania, laboratory studies gave the following results: Repeated routine blood counts and urinalyses showed no abnormality. The urine, tested on two occasions, showed no bromides or iodides. Several cultures for aerobic and anaerobic bacteria, fungi, amebas and tubercle bacilli were made of the blood, of fluid from the "abscesses" and of a biopsy specimen, and guinea pigs were inoculated with the first two substances. All the results were negative. The readings for the sugar content of the blood varied between 75 and 85 mg.; for urea nitrogen, between 10 and 12 mg., and for cholesterol, between 125 and 205 mg. per hundred cubic centimeters. Roentgenograms of the teeth, skull and chest showed no abnormality. Patch tests with iodides and bromides in the form of 50 per cent aqueous solution and as 12.5 per cent ointments gave negative results after twenty-four hours. The results of intracutaneous tests with oidiomycin and trichophytin were negative. Several Kolmer and Kahn serologic tests were negative. A Berkefeld filtrate of

fluid from an "abscess" injected intracutaneously and subcutaneously elicited no reaction. Tuberculin tests, performed by Dr. Carmen C. Thomas, gave the following results:

Amount	Test Substance [14]	Result
0.00002 mg.	purified protein derivative	plus 2
0.1 cc. 1:10,000	human sarcoid	plus 1 (?)
0.1 cc. 1:10,000	avian tubercle bacillus	negative
0.1 cc. 1:10,000	bovine tubercle bacillus	plus 4
0.1 cc. 1:1,000	human sarcoid	plus 2
0.1 cc. 1:1,000	avian tubercle bacillus	negative
0.1 cc. 1:100	human sarcoid	plus 4
0.1 cc. 1:100	avian tubercle bacillus	plus 4

Subcutaneous injections of 0.00002 mg. of purified protein derivative produced no reaction. A patch test with the no. 1 dilution of purified protein derivative showed a negative result after twenty-four hours.

On two occasions, when the disease was quiescent, the patient was given 5 grains (0.3 Gm.) each of potassium iodide and sodium bromide three times a day for one week. No exacerbation of the disease followed.

Two biopsy specimens were obtained, one from a lesion two days old and another from a lesion of six days' duration. Both were stained with hematoxylin and eosin. In the early specimen the epidermis was normal. The corium was the site of a moderate perivascular round cell infiltration, which was more pronounced in the deeper portions and was associated with vascular dilatation. This same process extended by way of the fibrous septums about the sweat glands and the deeper portions of the sweat ducts. The subcutaneous fatty tissue showed changes only in the neighborhood of the fibrous tissue. The intervening fat cells were apparently normal. The fibrous septums, however, were the sites of a round cell infiltrate which was dense and from which migration into the neighboring fat cells occurred. Here the fat cells became separated and suffered a partial loss of fat content, indicated by a periphery of cytoplasm and by the presence of a large vesicular nucleus set in a mass of lightly staining cytoplasm at one side of the diminished fat globule.

The sections obtained from the older lesion showed much more advanced pathologic change. Unfortunately, the epidermis and the corium were not present in these sections, which contained only a portion of the involved fatty tissue. Several fibrous septums were present and were the sites of a high grade of round cell infiltration, which extended into the fatty tissue on either side of these partitions. In the immediate proximity of the septums the fat cells, except in occasional isolated instances, had disappeared entirely and were replaced by a solid mass of globular cells containing large vesicular nuclei with prominent nucleoli. The cytoplasm of these cells was full of tiny droplets, so that the cells had the appearance of foam cells. These elements varied considerably in size. Some were as large as fat cells. While most of these elements contained only a single nucleus, many had two, and a few giant cells were present with as many

14. "Human sarcoid" refers to the tuberculin made from the critical R Miller phase of the tubercle bacillus, supplied to the clinic by R. R. Mellon and L. G. Beinhauer (Pathogenesis of Noncaseating Tuberculosis of the Skin and Lymph Glands, Arch. Dermat. & Syph. **36**:515-533 [Sept.] 1937), while the avian tuberculin is the tuberculin supplied by the same authors, made from critical R no. 2 phase of the avian tubercle bacillus.

as twenty-five nuclei. The giant cells were of the foreign body type, as the nuclei were centrally and irregularly placed. Their cytoplasm, like that of their neighbors, presented a "foamy" appearance. Between these foam cells many lymphocytes and a few polymorphonuclear cells were seen. In many instances even the cytoplasm of these cells presented a "foamy" appearance. Here and there throughout the infiltrate were large round spaces, presumably the sites of collections of free fat. In the fatty tissue, farther removed from the fibrous septums, many normal fat cells were present. On the other hand, all transitional stages could be traced between the normal fat and the dense inflammatory infil-

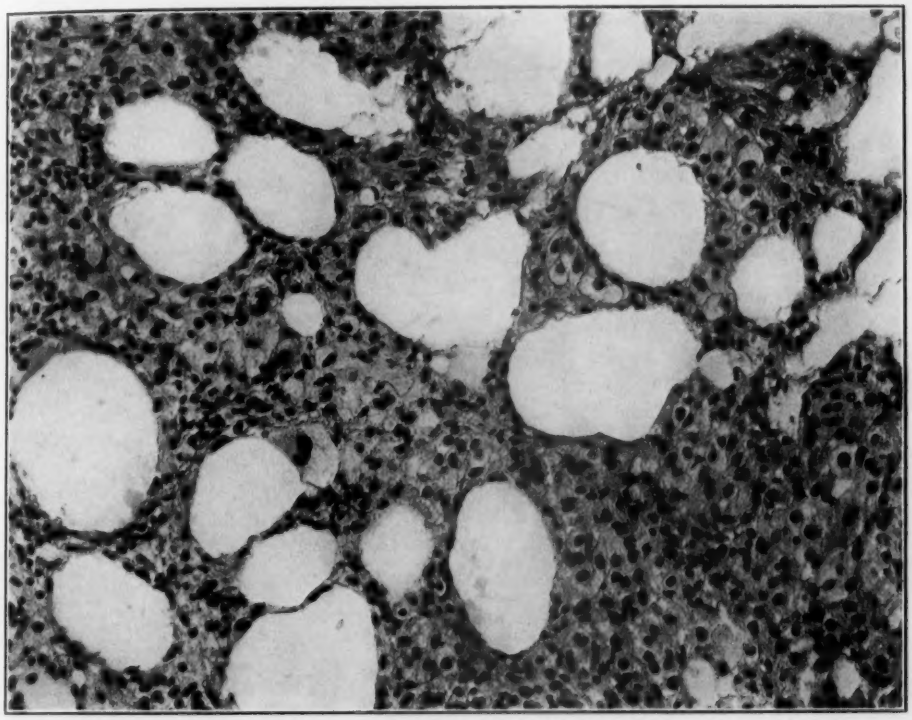

Fig. 2.—Photomicrograph (× 240) of a lesion 6 days old, showing the round cell infiltrate and the massed collection of foam cells, many of which contain more than one nucleus. Only a few fat cells are present. The fat globule in one of these (upper right-hand corner) is undergoing resorption. The large open spaces presumably represent collections of free fat.

trate with foam cell structures in the sites where the pathologic process was most marked. Near one of the fibrous septums the outlines of the foam cells could no longer be distinguished, so that the section presented the appearance of large numbers of vesicular nuclei disposed in an amorphous foamy matrix. At this place the inflammatory infiltrate was most marked, and the polymorphonuclear cells were most numerous. Evidently this was a site at which liquefaction of the fatty tissue was about to occur. Throughout the whole of the section the blood vessels were greatly dilated.

During the first few weeks of her stay in the hospital the patient's course was steadily downhill. The lesions became larger and very numerous. She refused most of her food and lost a great deal of weight.

On Dec. 18, 1936, treatment with neoarsphenamine, 0.3 Gm. twice a week, was started. The patient almost immediately made a favorable response. No new lesions appeared, and the temperature fell to normal. Unfortunately, this improvement proved to be only temporary; within four weeks (on Jan. 18, 1937), while she was still under treatment with neoarsphenamine, the lesions recurred, and the temperature, which had remained almost normal, began to climb again. Subsequently treatment with sodium gold thiosulfate was begun, and a similarly favorable but less dramatic course followed. Treatment consisted of ten weekly intravenous injections of from 25 to 50 mg. of the drug; as in the case of neoarsphenamine, the effect of the gold salt was only temporary.

From April until November 1937 the patient, while being treated with a second short course of neoarsphenamine and of sodium gold thiosulfate, slowly but progressively improved. Altogether, the patient received a total of 6 Gm. of neoarsphenamine and 700 mg. of sodium gold thiosulfate.

From November 1937 until February 1938 only a few lesions appeared; there were none in the six weeks preceding this report.

COMMENT

Although superficially there are many points of resemblance between the condition described here and relapsing febrile nonsuppurative nodular panniculitis, on closer examination many differentiating features stand out. The most obvious difference is the fact that in the case reported the lesions broke down and underwent liquefaction with subsequent rupture and discharge, while in the Weber-Christian syndrome the lesions undergo spontaneous absorption and involution. Other differentiating points can be noted. In relapsing febrile nonsuppurative nodular panniculitis the lesions are usually not painful or tender. The skin over the lesions may retain its normal color. The distribution of the lesions is more extensive and as a rule involves the trunk. Each crop of lesions is usually accompanied with a sharp febrile response. On the other hand, in the case reported the lesions were painful and tender, and the skin over them eventually became involved and assumed an erythematous, and later a cyanotic, color. The lesions were confined to the buttocks and the extremities. At no time were they present on the trunk proper. The febrile response in this case seemed to be less marked and to follow less closely the appearance of new lesions than in Weber-Christian disease. It is to be noted that the patient's febrile response, while present when the lesions were most numerous and most active, was absent during the last eight months of the disease, even though new lesions, albeit in smaller crops, continued to appear. One gets the impression from reading the literature that the febrile response is a much more constant accompaniment of even small showers of new lesions in Weber-Christian disease than it was in the case reported here.

Subcutaneous fat necrosis is differentiated from the condition described by the fact that fever, liquefaction of lesions, involvement of the skin, pain and tenderness, numerous and widespread distribution of the lesions, rapid evolution and repeated appearance of new lesions —all features of the latter condition—are absent in the former diease.

Other diseases with involvement of the subcutaneous fatty tissue, such as erythema nodosum, erythema induratum, phlebitis, tuberculosis of the hypoderm, sarcoidosis, nodular syphilis, deep-seated fungous infection, amoebiasis cutis, drug (bromide or iodide) eruption and neoplastic disease, could all be ruled out on the basis of appropriate clinical, laboratory and histologic studies.

I was unable to determine the cause of this condition, in spite of the studies detailed in this report. The clinical picture strikes one as an unusually active type of lipolytic response in the subcutaneous fatty tissue to some hematogenously disseminated noxa.

The extensive tuberculin tests, with types of tuberculin derived from various sources, demonstrated only the grade of allergic response prevalent in most adults in the patient's locality. Perhaps the reaction to the bovine tuberculin was more marked than one would expect, but this had no diagnostic value, since bovine and human tuberculin are supposed to react interchangeably. At least it can be said that anergy to any type of tuberculin did not exist in this case, so that a sarcoid-like reaction can be ruled out.

Unfortunately, methods were not available for the study of the role of filtrable viruses in this process, but a Berkefeld filtrate of the aspirated contents of an early lesion failed to produce a reaction when injected intracutaneously or subcutaneously.

Furthermore, a careful study of the sections failed to show any of the more or less characteristic features often seen in virus diseases, such as balloon degeneration and inclusion bodies.

SUMMARY

A case of liquefying nodular panniculitis, which, so far as I can determine, has not been described before, is reported. The essential clinical features are (1) appearance of deep-seated, painful and tender, woody nodules in the subcutaneous fatty tissue; (2) their evolution in from seven to ten days into cystic masses containing from 1 to 4 ounces (30 to 120 cc.) of an oily or fatty yellowish brown fluid; (3) the fact that just before rupture (ten to fourteen days) the skin overlying the mass was livid and raised, while the central portion was attenuated into a thin translucent bulla-like membrane, through which underlying fluid could be easily discerned; (4) the formation of a deep cuplike depression in the subcutaneous fat, associated with a thin puckered scar,

at the site of the healed lesion; (5) the presence of fever when the active lesions were most numerous, although many crops of lesions appeared when the temperature was normal, and (6) the distribution of the lesions exclusively on the buttocks and extremities and most markedly on the buttocks and lower extremities.

The histologic features of the process are (1) a primary round cell infiltrate beginning in the fibrous septums and spreading out to involve the neighboring fat cells; (2) the disappearance of the fat cells and their replacement by foam cells containing one or more vesicular nuclei; (3) the eventual liquefaction of the process, as demonstrated by the loss of outline by the foam cells and its replacement by an amorphous foamy matrix in which the vesicular nuclei as well as the inflammatory round and polymorphonuclear cells are suspended.

PARAPSORIASIS EN PLAQUES DISSÉMINÉES AND INCIPIENT MYCOSIS FUNGOIDES

SUPPLEMENTARY DATA ON THEIR RELATIONSHIP

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In my article on the relation between parapsoriasis en plaques disséminées and incipient mycosis fungoides [1] it was suggested that the former dermatosis probably is the precursor of the latter disease in most if not all cases. It was further implied that parapsoriasis en plaques disséminées, parapsoriasis "lichenoides" of French authors, parakeratosis variegata (Unna, Santi and Pollitzer) and the retiform type of parapsoriasis with its transitions to "poikiloderma" are, in all likelihood, phases of a single condition terminating in mycosis fungoides in the vast majority of instances; that these dermatoses are distinct from parapsoriasis guttata (pityriasis lichenoides chronica of Juliusberg) and the group of parapsoriasis varioliformis, the latter two diseases showing no tendency to evolve into mycosis fungoides; and that a defective nomenclature has been responsible, in part at least, for the inclusion of unrelated conditions in one category. These statements find direct confirmation in the prophetic opinions voiced by Wile many years ago in the course of several discussions.[2]

It is now my privilege to furnish many additional references, besides those found in the previously mentioned article, in substantiation of these conclusions, which I now believe were too conservatively stated. This is being done for three reasons: 1. Chwatt [3] has recently published a general review of the question, and, although it is evident that that observer had misgivings regarding the nature of the relationship, he considered the evidence collected in his communication insufficient to warrant drawing conclusions; his review, however, lacked much material which may be found in my previous paper. 2. Several references in my

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1. Keil, H.: Parapsoriasis en Placques Disséminées and Incipient Mycosis Fungoides, Arch. Dermat. & Syph. **37**:465 (March) 1938.

2. Wile, U. J., (*a*) in discussion on Ormsby, O. S.: Parapsoriasis (Brocq), Arch. Dermat. & Syph. **12**:563 (Oct.) 1925; (*b*) in discussion on Ormsby, O. S.: Parapsoriasis with Leukemia, ibid. **13**:690 (May) 1926.

3. Chwatt, L.: Bull. Soc. franç. de dermat. et syph. (Réunion dermat., Strasbourg) **44**:1354, 1937.

first article may now be presented with more complete data. 3. As part of the data were obtained accidentally, it seems worth while to record information on the ultimate fate of a condition that in many instances pursues a monotonous course for many years before definite changes in the clinical picture occur. Even now the references will necessarily be incomplete, as I am concerned chiefly with the American literature in the past twenty years (1917-1937). For convenience the new cases will be grouped under several categories, and brief abstracts of the chief points of interest will be appended. As the clinical picture is variable, the classification of any particular example of the condition will depend, in great part, on the time of observation and the views held by the individual observer.

A. PARAPSORIASIS EN PLAQUES DISSÉMINÉES TERMINATING IN MYCOSIS FUNGOIDES

(a) *Cases in Which the Diagnosis Was Definite.*—1. Sevin [4] reported the case of a man 48 years old who had had cutaneous lesions for twenty-four years. In 1921, at the Stuttgart Congress, the condition was diagnosed as lichen ruber acuminatus; in 1931, as Brocq's parapsoriasis. For the last two years the patient had presented the typical picture of extensive mycosis fungoides. Hence, about twenty years elapsed before a definite transformation occurred.

2. Fox [5] presented a man aged 49 who had had an eruption for at least thirty years. There had been no itching for twenty-five years. The pathologic changes, according to Dr. T. J. Riordan, were those of a chronic inflammatory process, possibly mycosis fungoides. In the discussion G. M. MacKee pointed out the clinical resemblances of the condition to parapsoriasis but stated that the minute anatomic alterations favored the diagnosis of mycosis fungoides. Perusal of the pathologic report shows data that appear to substantiate this opinion (the sharp inferior margin of the infiltrate, the nature of the cellular response, the suggestion of cell nests in the epidermis, etc.).

3. In a discussion of Garner's [6] case, A. Strauss and C. S. Wright expressed the belief that the eruption was incipient mycosis fungoides (horseshoe-shaped configurations, a tendency of some lesions to be thickened and severe pruritus). Dr. F. D. Weidman said:

in this case there is lacking something almost constant in mycosis fungoides, namely, edema and swelling of the epidermal cells, and these cells generally have conspicuous prickles. The cells infiltrated in the corium are polymorphous, many

4. Sevin: Zentralbl. f. Haut- u. Geschlechtskr. **50**:273, 1935.

5. Fox, H.: A Case for Diagnosis (Poikiloderma?), Arch. Dermat. & Syph. **32**:975 (Dec.) 1935.

6. Garner, V. C.: A Case of Parapsoriasis en Plaques Disséminées, Arch. Dermat. & Syph. **24**:1098 (Dec.) 1931.

have highly chromatic nuclei, and many are endothelioid—factors in harmony with mycosis fungoides. Things are thus so conflicting that I am afraid this is a case in which the histology does not get us very far.

It is my belief that, though this case was presented as one of Crocker's xanthoerythroderma perstans, the weight of evidence preponderates in favor of mycosis fungoides in its early stages.

4. Ormsby [7] stated that he had observed 3 cases of Brocq's type of parapsoriasis associated with potential lymphatic leukemia. After observing the patients for several years, he was unable to adduce a connection between the condition of the blood and the cutaneous changes. These cases must now be evaluated in the light of the data collected here and in my previous paper.

Wile,[2n] discussing the features of one of the cases mentioned by Ormsby, remarked that the case showed "a connecting link between parapsoriasis and the malignant lymphomas, particularly those which develop into granuloma fungoides." In the discussion Ormsby mentioned that for several years he had observed 2 examples of what was apparently parapsoriasis in which there was little itching, and that the picture of mycosis fungoides later developed. I have been unable to trace these examples.

Wile,[2b] discussing the same case a year later, uttered another opinion with which I am in entire accord:

I believe we are very soon coming to the point where we must take out from the benign group of parapsoriases the so-called en plaque forms. I have come to regard every case of parapsoriasis en plaque as potentially serious. . . . I personally can see absolutely no real relation between the disseminated plaque form of so-called parapsoriasis and the guttate type or pityriasis lichenoides chronica.

5. Pels [8] reported the case of a man aged 37 who had had an eruption for sixteen years. There had been a temporary response to ultraviolet radiation. Histologic examination showed only superficial changes; there was thickening of the rete, acanthosis, parakeratosis and slight subpapillary edema. This case was apparently accepted as an authentic example of the condition. Addendum: In the course of a discussion at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital in March 1938, Cipollaro mentioned what seemed to be the case presented by Pels. As I am not certain of the identity, however, I am giving the brief notes which Cipollaro [9] furnished. The case was that of a man of 46 who had previously been under the observation of Dr. Pels. The eruption had a duration of twenty-five years and had occasionally responded favorably to ultraviolet radiation. At

7. Ormsby, O. S., in discussion on Wile, U. J., and others: Mycosis Fungoides with Poikiloderma-Like Changes, Arch. Dermat. & Syph. **36**:898 (Oct.) 1937.

8. Pels: Parapsoriasis Erythrodermie Pityriasique en Plaques Disséminées, Arch. Dermat. & Syph. **16**:647 (Nov.) 1927.

9. Cipollaro, A.: Personal communication to the author, March 23, 1938.

the time of the report there were some infiltrated patches on the buttocks and the legs, and some of these were ulcerated. The lesions responded remarkably to 1 or 2 roentgen treatments (75 r unfiltered). Dr. Cipollaro stated: "Clinically the infiltrated patches appearing on patches of clinical parapsoriasis have the appearance and behavior of mycosis fungoides."

6. Templeton [10] stated that he recalled a case presented by Klauder as an instance of parapsoriasis en plaques disséminées in which the condition later developed into mycosis fungoides. I have been unable to trace this case.

7. Scheer [11] informed me that of the half-dozen cases of parapsoriasis in patches observed by him many years ago, most of them being in private practice, the clinical features of mycosis fungoides developed in all; this information was gained from several sources accidentally. Dr. Scheer was unable to supply me with specific protocols.

(b) *Cases in Which There Were Features Suggestive of Mycosis Fungoides.*—8. In the discussion of Chipman's [12] case, H. J. Templeton pointed out that the pruritus suggested the diagnosis of mycosis fungoides, and Howard Morrow expressed agreement with this suggestion.

9. In discussing Gross's [13] case, S. Pollitzer expressed the belief that the marked redness of the patches, the involvement of the face and the considerable itching were points favoring a diagnosis of mycosis fungoides. Gross agreed with these observations but noted that the histologic changes were not those of mycosis fungoides. Pollitzer, however, remarked that, although the typical alterations of mycosis fungoides may be absent, they subsequently develop.

10. The case reported by Hopkins [14] with the tentative diagnosis of parapsoriasis had been previously reported by Wise [15] as an instance of parapsoriasis en plaque. In 1923 the histologic examination revealed changes apparently consistent with parapsoriasis. According to J. G. Hopkins, the question of parapsoriasis versus mycosis fungoides was debated on this occasion. In 1928 there was still a difference of opinion. Jerome Kingsbury regarded the case as one of parapsoriasis. Louis

10. Templeton, H. J., in discussion on Chipman, E. D.: Parapsoriasis (Brocq Type), Arch. Dermat. & Syph. **21**:315 (Feb.) 1930.

11. Scheer, M.: Personal communication to the author.

12. Chipman, E. D.: Parapsoriasis (Brocq Type), Arch. Dermat. & Syph. **21**:315 (Feb.) 1930.

13. Gross, P.: Parapsoriasis and Grenz-Ray Sequelae, Arch. Dermat. & Syph. **20**:251 (Aug.) 1929.

14. Hopkins, J. G.: A Case for Diagnosis (Parapsoriasis?), Arch. Dermat. & Syph. **17**:562 (April) 1928.

15. Wise, F.: Parapsoriasis en Placque, Arch. Dermat. & Syph. **8**:440 (Sept.) 1923.

Chargin and O. L. Levin considered it one of incipient mycosis fungoides, in view of the central clear areas in some patches, the history of recurrent attacks and the infiltration in and well defined borders of some lesions. The histologic report was again not conclusive; there were parakeratosis, to which the thickening in some of the patches was attributed, a slight perivascular infiltration with lymphocytes and young connective tissue cells and a few fragmented nuclei—in insufficient numbers, however, to point definitely to mycosis fungoides.

11. Littman [16] reported the case of a man of 50 who had had an eruption for eighteen years. One patch on the thigh was infiltrated. H. M. Cole stated that, despite the long course and the lack of itching, the indurated area on the thigh suggested the diagnosis of mycosis fungoides.

12. Scheer [17] presented a case of parapsoriasis (Brocq type). P. E. Bechet pointed out that two or three patches on the trunk, which were sharply defined, with a marked serpiginous outline and slight infiltration, warranted a careful watch for the possible development of mycosis fungoides. This case can now be evaluated in terms of the information given to me by Scheer.[11]

13. Wise [18] reported the case of a man of 69 who had had an eruption for four years. One side of the body was treated with roentgen radiation and responded to this form of therapy. G. M. MacKee regarded this as grounds for suspecting mycosis fungoides.

14. Turnacliff [19] reported the case of a patient aged 68 who suffered from severe itching in connection with his eruption.

B. PARAKERATOSIS VARIEGATA

(a) *Supplementary Notes.*—15. Nekam [20] stated, on the authority of Pautrier, that Brocq toward the latter part of his life was entirely dissatisfied with the status of his cases of parapsoriasis "lichenoides" and advised further study of them.

16. Civatte, discussing the instance of "parakeratosis variegata" presented by Sézary, Civatte and Horowitz,[21] stated that in the case of parakeratosis variegata which he observed jointly with Brocq in 1905

16. Littman: Parapsoriasis en Placques, Arch. Dermat. & Syph. **20**:421 (Sept.) 1929.

17. Scheer, M.: Parapsoriasis (Brocq Type), Arch. Dermat. & Syph. **13**:268 (Feb.) 1926.

18. Wise, F.: Parapsoriasis en Placques, Arch. Dermat. & Syph. **15**:625 (May) 1927.

19. Turnacliff: Parapsoriasis, Arch. Dermat. & Syph. **14**:744 (Dec.) 1926.

20. Nekam, L., Jr.: Ann. de dermat. et syph. **9**:31, 1938.

21. Sézary, A.; Civatte, A., and Horowitz, A.: Bull. Soc. franç. de dermat. et syph. **39**:1220, 1932.

mycosis fungoides had developed. Civatte probably referred to observation 23 in his thesis,[22] made in a case originally regarded by him as possibly one of mycosis fungoides. Among the remarks made by Civatte in 1932, the following are of great interest: "Can this be a premycotic eruption in all cases? I do not know. I hope not."

17. S. Pollitzer, discussing Chipman's paper [23] stated that Santi's case of "parakeratosis variegata" subsequently evolved into one of mycosis fungoides. He stated in February 1937 [24] that he did not know the ultimate outcome in his case, but he did remember that in neither instance forming the basis of the report by Unna, Santi and Pollitzer (1890) [25] was there anatomic evidence of mycosis fungoides at the time of examination.

(b) *Additional Cases.*—18. Bogrow [26] reported the case of a woman of 36 who had had an eruption for eight years. There was a typical picture of parakeratosis variegata. On the trunk there were, in addition, two "tomato tumors," regarded as evidence of mycosis fungoides. Examination of the blood showed 7.9 per cent eosinophils.

19. Savatard [27] reported the case of a woman 62 years old who had had an eruption for forty-one years. On the trunk the lesions were "very suggestive of parakeratosis variegata." The left scapula was the site of a raised, circumscribed and infiltrated mass, which was not ulcerated. Specimens from a fungating ulcer in the left supraclavicular region and from one on the left thigh showed the anatomic features of mycosis fungoides. The ulcerated area had been present only seven weeks. Savatard referred to one of Jamieson's [28] cases, in which a diagnosis of parakeratosis variegata was made by Unna and in which the clinical picture of mycosis fungoides later developed. Savatard's case is remarkable for the long duration of the disease, the insignificant pruritus and the features of "parakeratosis variegata."

C. "POIKILODERMA" TERMINATING IN MYCOSIS FUNGOIDES

That cases may be classified variously as instances of parapsoriasis in patches, of poikiloderma, of parakeratosis variegata, of parapsoriasis "lichenoides" or of mycosis fungoides has been noted in many reports. In addition to those already mentioned in my previous paper, there have

22. Civatte, A.: Les parapsoriasis de Brocq, Thesis, Paris, no. 216, Paris, G. Steinheil, 1906.

23. Chipman, E. D.: Parapsoriasis, Arch. Dermat. & Syph. **4**:807 (Dec.) 1921.

24. Pollitzer, S.: Personal communication to the author.

25. Unna, Santi and Pollitzer, cited by Pollitzer.[24]

26. Bogrow, S.: Arch. f. Dermat. u. Syph. **107**:471, 1911.

27. Savatard: Brit. J. Dermat. **50**:150, 1938.

28. Jamieson, W. A., in Encyclopaedia Medica, Edinburgh, W. Green & Sons, 1900, vol. 6, p. 450.

been several publications bearing on this subject. It must be emphasized that I am concerned only with one type of "poikiloderma" and that this variety appears to differ from several other conditions commonly grouped in this category; this subject will be discussed in greater detail in another publication.

20. Oliver [29] made an outstanding report of a single example and supplied a fairly complete review of the cases in the literature.

21. The members of Wile's [30] clinic presented a case of mycosis fungoides with poikiloderma-like changes. In a discussion of this example of the condition, H. Pinkus mentioned the case of a man of 50 whose condition had been diagnosed as poikiloderma in Jadassohn's clinic in Breslau, Germany, several years before. It is extremely interesting that twenty years before that Neisser had classified the case as one of "pityriasis lichenoides chronica." (This may well have been "lichenoid" parapsoriasis or parakeratosis variegata.) In 1931 the diagnosis of poikiloderma was discussed, and one year later the typical tumors of mycosis fungoides appeared.

22. Fox [31] reported a case which had been previously presented on several occasions [32] and accepted as a typical example of the condition. The histologic changes were apparently not those of mycosis fungoides or of lymphoblastoma in 1931. In 1937 there were dull red, firm nodules and diffuse plaques, chiefly on the forehead, and the pathologic alterations were regarded as those of lymphoblastoma. It is probable that the changes were consistent with the belief that the patient had mycosis fungoides. In 1932 or 1933 I had the opportunity of observing this patient and likewise thought the condition typical of what has been described in textbooks as poikiloderma vasculare atrophicans. This case is of fundamental interest for at least two reasons: (1) the transformation did not occur until twelve years after the onset, and (2) the diagnosis of poikiloderma vasculare atrophicans was unanimously accepted by a host of competent dermatologists. The absence of itching was an outstanding feature.

23. Lane [33] reported a case which he regarded as showing the features of poikiloderma. A disturbing element was the presence of a tumor on the dorsum of the left foot. Kingsbury expressed the belief

29. Oliver, E. A.: Mycosis Fungoides with Poikiloderma-Like Symptoms, Arch. Dermat. & Syph. **33**:267 (Feb.) 1936.

30. Wile, U. J., and others: Mycosis Fungoides with Poikiloderma-Like Changes, Arch. Dermat. & Syph. **36**:898 (Oct.) 1937.

31. Fox, H.: Poikiloderma Vasculare Atrophicans and Lymphoblastoma, Arch. Dermat. & Syph. **35**:549 (March) 1937.

32. Oulmann, L.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **23**:363 (Feb.) 1931.

33. Lane, J. E.: Poikiloderma, Arch. Dermat. & Syph. **15**:621 (May) 1927.

that the condition was mycosis fungoides. In a later report of the same case [34] it was stated that the tumor showed the microscopic picture of mycosis fungoides. This fact was later referred to in other reports,[35] in which it was stated that the tumors began to evolve rapidly.

24. Lane [36] presented a well known case which terminated as an example of Hodgkin's disease. For several reasons, however, acceptance of that diagnosis is somewhat problematic: 1. In discussing this example, Lane [33] stated that "the tumors were probably Hodgkin's disease, though the pathologists would not make a positive diagnosis." 2. Tumors occur in the skin more commonly in mycosis fungoides than in Hodgkin's disease. If the poikiloderma is regarded as the precursor of the final condition, as Lane surmised, the patient had the disease for over fourteen years; this is a duration observed more often in cases of mycosis fungoides. 3. General pathologists experienced great difficulties in differentiating Hodgkin's disease from mycosis fungoides. In Lane's case, for example, the involved glands did not show areas of necrosis or of fibrosis, changes to be expected in the average example of Hodgkin's disease of such duration. The alterations, especially those in the internal organs, as in a case studied by me in 1930, may be so similar in these conditions as to render the differentiation more a clinical than an anatomic problem. Indeed, some pathologists are inclined not to separate these diseases.

25. Ormsby's [37] case of poikiloderma was included in Lane's paper.[36b] However, a complete report of the original findings was not appended, and, as some of the changes appear to be important, they will be mentioned here. The patient, aged 33, had apparently had the condition since childhood. A few months before the presentation, two hard tumors appeared on the back, and the patient showed the scars of their excision; the pathologic changes in these tumors were not reported. It is interesting that there were eosinophilia (10 per cent eosinophils) and slight leukocytosis. Ormsby was consulted because of an indurated lesion involving the penis. Regional glandular involvement was noted. The subsequent history of the disease "proved it to be lymphosarcoma which became generalized by metastatic involvement of the abdominal

34. Lane, J. E.: Poikiloderma (?), Arch. Dermat. & Syph. **16**:117 (July) 1927.

35. (*a*) Keim, H. L.: The Lymphoblastomas: Their Interrelationships, Arch. Dermat. & Syph. **19**:533 (April) 1929. (*b*) Lane, J. E., in discussion on Larocco, C. G., and Cummer, C. L.: Poikiloderma Atrophicans Vasculare, ibid. **23**:174 (Jan.) 1931.

36. Lane, J. E.: (*a*) Poikiloderma Atrophicans Vasculare, with Report of a Case by Oliver S. Ormsby, Arch. Dermat. & Syph. **4**:563 (Nov.) 1921; (*b*) Poikiloderma Atrophicans Vasculare: Conclusion of Previously Reported Case, ibid. **8**:373 (Sept.) 1923.

37. Ormsby, O. S.: J. Cutan. Dis. **35**:42, 1917.

and thoracic regions, terminating fatally in one year." So far as I can ascertain, postmortem examination was not made. Ormsby [38] expressed the belief that there was no connection between the development of the lymphosarcoma and the poikiloderma, but in view of the data presented here and in my previous paper, it seems possible that a closer relation existed than had been considered. The occurrence of two unusual conditions in the same patient may be coincidental, but such combinations warrant at least a suspicion of a relation. In addition, there was already present in 1917 an unexplained eosinophilia and a statement in the history that the original section of the lesion on the penis "showed it to be inflammatory and not epitheliomatous."

26. Ormsby [39] observed large areas of "idiopathic atrophy" following the disappearance of patches of mycosis fungoides, these lesions resembling poikiloderma; such appearances are not rare.

27. Keim [35a] cited cases 7 and 11 as examples of "lymphoblastomas" showing poikiloderma-like changes in the skin.

28. A member of the staff of the Cincinnati General Hospital presented a case of poikiloderma [40] in a woman aged 52 who had an eruption that apparently had its onset some thirty-one years before. There was pruritus. The first histologic examination showed "a rather diffuse infiltration of lymphocytes." The dermatosis did not respond to ultraviolet irradiation. At one time there appeared numerous pruriginous papules "which biopsy showed to be lymphocytic granulomas." These lesions responded promptly to roentgen irradiation. In the discussion of this case J. M. Markin stated that "the response of the nodules to roentgen therapy and the results of the histologic examination are suggestive of mycosis fungoides." H. R. Foerster noted the presence of infiltrated exudative plaques on the back, the lesions suggesting that the condition belonged in the lymphoblastoma group.

29. Perlstein [41] presented a case of apparently typical poikiloderma in its accepted sense. In the discussion O. H. Foerster pointed out the arcual character of the superficial infiltrates on the back and arm, these lesions resembling mycosis fungoides.

30. Bancroft [42] presented a woman aged 44 who had had an eruption for twenty years. Originally it had not been pruritic, but as the condition spread, itching became severe. At first Bancroft thought the dis-

38. Ormsby, O. S., in discussion on Oliver.[29]

39. Ormsby, O. S., cited by Oliver.[29]

40. Poikiloderma (Jacobi), Arch. Dermat. & Syph. **34**:165 (July) 1936.

41. Perlstein, M. O.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **28**:735 (Nov.) 1933.

42. Bancroft, I. R.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **27**:540 (March) 1933.

ease was mycosis fungoides, but at the time of presentation he expressed the belief that it was poikiloderma vasculare atrophicans. M. Scholtz expressed the belief that it was parapsoriasis, possibly progressing into mycosis fungoides.

31. Whitehouse [43] reported the case of a woman of 34 who had had an eruption for thirteen years. In the past three years an ulcerated area had appeared on the right side of the neck; this lesion healed during the use of ichthammol ointment. About one year before presentation the arms and the legs had been the sites of an eruption resembling "mycosis." The lesions became red and indurated and disappeared in a few days, leaving pigmentation; they recurred at short intervals. Ten years before all the patches had disappeared after the use of "drops." The histologic report was noncommittal, but apparently early mycosis fungoides was considered. Four treatments with roentgen radiation did not produce any apparent effect.

SUMMARY AND CONCLUSIONS

1. Parapsoriasis in patches, parapsoriasis "lichenoides" of French authors, parakeratosis variegata and the retiform type of parapsoriasis with its transitions into "poikiloderma" probably represent phases of a single condition that terminates in mycosis fungoides.

2. These types of so-called parapsoriasis are to be differentiated sharply from pityriasis lichenoides chronica (parapsoriasis guttata) and the group of parapsoriasis varioliformis.

3. The conception of parapsoriasis, of mycosis fungoides and of poikiloderma vasculare atrophicans require revision in the light of the collected data.

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43. Whitehouse, H. H.: Poikiloderma Atrophicans Vasculare, Arch. Dermat. & Syph. **7**:836 (June) 1923.

JUVENILE PEMPHIGUS

EFFECTS OF GERMANIN * IN THREE CASES

C. C. TOMLINSON, M.D.

WITH THE COLLABORATION OF

O. J. CAMERON, M.D.

OMAHA

Germanin was introduced in 1928 by Kleine [1] for the treatment of trypanosomiasis, in which it has been somewhat effective. Veiel [2] in 1931 first suggested the use of germanin in the treatment of pemphigus, reporting 3 cures among 4 cases. Fabián [3] in 1933 reported the clinical cure of pemphigus in a boy 4 years old after four injections of germanin, after other measures had been ineffective. An elderly woman with diabetes and pemphigus was treated with this drug by Fabián; a high fever developed, and the patient died after the third injection. In the same year Zoon [4] reported the use of germanin in a case of pemphigus; there was rapid healing of lesions, followed by a recurrence in six months which proved fatal in spite of further medication. Zoon gave germanin also to 6 patients afflicted with dermatitis herpetiformis. There were a favorable response in 5 cases and death in 1. Zoon pointed out that

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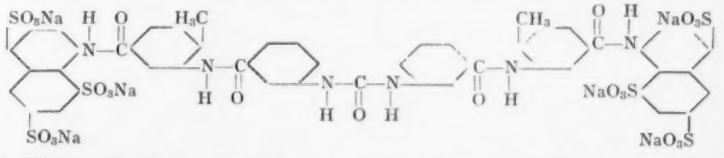
*Germanin (Bayer 205) is a foreign proprietary preparation and has not been submitted to the Council on Pharmacy and Chemistry of the American Medical Association or examined by its laboratory. The Winthrop Chemical Company, American representative of the manufacturer, gives the following information: Germanin is chemically a sodium salt of sym. bis. (*m*-aminobenzoyl-*m*-amino-*p*-methylbenzoyl-l-naphthylamino-4,6,8-trisulfonic acid) urea. It is therefore a complex organic combination containing no arsenic, antimony, bismuth or mercury. The structural formula is as follows:



1. Kleine, F. K.: Final Report of the League of Nations International Commission on Human Trypanosomiasis, Boston, World Peace Foundation, 1928.

2. Veiel, F.: München. med Wchnschr. **78**:2047 (Nov. 27) 1931.

3. Fabián, A.: Česká dermat. **14**:137, 1933.

4. Zoon, J. J.: Acta dermat.-venereol. **14**:473 (Dec.) 1933.

after-effects were fever, albuminuria, toxic erythema and nausea, but that these effects were usually transitory. Bode [5] (1933) reported 3 cases of pemphigus in which there was no benefit from germanin. Dowling [6] (1934) reported the cure of pemphigus in a woman aged 66 with small doses (0.5 Gm.) of germanin three times weekly. Inoue [7] (1934) reported on the use of germanin (total dosage 5 Gm.) in a case of pemphigus chronicus pruriginosus. The eruption healed rapidly and completely, although all other remedies had been ineffective. Tobias [8] (1934) treated a girl of 5 years in whom typical juvenile pemphigus had developed after scarlet fever. Although the commonly used therapeutic measures, including administration of a blood-coagulating preparation, intramuscular injection of milk, the use of acetarsone, of hot air, of potassium arsenite and of viosterol, ultraviolet irradiation, bathing with hypertonic saline solution and potassium permanganate and a diet high in vitamins were of no avail, treatment with germanin produced rapid healing of the lesions. The patient died suddenly, however, of acute endocarditis and sepsis. Sulzberger [9] (1935) presented before the Bronx Dermatological Society a Jewess aged 36, whom he had treated for pemphigus with germanin. She had shown both cutaneous and oral lesions. After the third injection of germanin a temperature of 105 F. and nephritis developed. Germanin was then given in conjunction with a liver extract and was well tolerated. Fourteen days after the sixth injection of germanin the pemphigus was entirely healed.

Aretz [10] (1935) reported cure in 2 cases of pemphigus following the use of germanin. In both cases the eruption involved the skin but not the mucous membranes. In 4 other cases of pemphigus involving both the skin and the mucosa, the drug was ineffective.

Geyer [11] in 1935 reported agranulocytosis following germanin therapy.

Donges [12] in 1936 published reports of 4 cases in which pemphigus was cured promptly with germanin, in 1 of which the patient's condition was apparently hopeless when he was first seen. The drug was given intramuscularly by this author, who believed less renal damage would occur from administration by this method than from intravenous use.

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5. Bode, H. G.: Dermat. Wchnschr. **97**:1160 (Aug. 5) 1933.
6. Dowling, G. B.: Proc. Roy. Soc. Med. **28**:109 (Dec.) 1934.
7. Inoue, N.: Hifu-to-Hitsungo **2**:323 (Aug.) 1934.
8. Tobias, N.: Juvenile Pemphigus: Treatment with Germanin (Bayer 205); Report of a Fatal Case, Am. J. Dis. Child. **48**:1084 (Nov.) 1934.
9. Sulzberger, M. B.: Pemphigus (Cured?), Arch. Dermat. & Syph. **32**: 517 (Sept.) 1935.
10. Aretz, H.: Dermat. Wchnschr. **100**:417 (April 13) 1935.
11. Geyer, H.: Acta dermat.-venereol. **16**:328 (Nov.) 1935.
12. Donges, R.: Dermat. Wchnschr. **102**:277 (March) 1936.

Michelson[13] (1937) showed before the Minnesota Dermatologic Society a man aged 52 with pemphigus who had received fifteen 1 Gm. injections of germanin in six weeks. The eruption healed rapidly, but erythematopapular toxic erythema resulted and the urine showed at times some casts and traces of albumin and sugar. In discussion, Michelson said that he had had good results from germanin in 1 case of pemphigus and in 3 cases of dermatitis herpetiformis. Becker[14] stated that 5 patients with pemphigus had received germanin therapy in Chicago; 1 patient had had temporary improvement but later died of Addison's disease, the autopsy showing complete atrophy of the adrenal cortex. This fatal result of therapy was recorded in 1937 by Wells, Humphreys and Work,[15] who concluded that the chemotoxic effect of prolonged germanin therapy had resulted in atrophy of the adrenal cortex and death of Addison's disease. They demonstrated that large doses of germanin given to rats, rabbits and guinea pigs caused serious injury to the kidneys, the liver, the myocardium, and the adrenal glands. With smaller doses it was found that the kidneys and the adrenal glands were injured to a greater extent than the liver or the myocardium. In a few guinea pigs renal changes were slight when the adrenal glands were seriously damaged. The adrenal glands usually showed a wide band of necrosis in the fasciculate zone of the cortex.

Vámos and Böhm[16] administered germanin to rats and rabbits and reported degenerative changes in the kidneys, the liver and the spleen.

Dennie[17] had a favorable response to germanin therapy in a case of pemphigus vulgaris.

Kinnear[18] (1938) reported on the use of germanin in 7 cases of pemphigus. Two children, aged 3 and 15 years, respectively, recovered; 1 patient with pemphigus vulgaris and 1 with pemphigus foliaceus died; 2 with acute pemphigus ushered in by erythema multiforme died, and 1 who presented evidence of possible combined pemphigus and dermatitis herpetiformis recovered.

From the foregoing review of the more pertinent literature on the use of germanin in the treatment of pemphigus, it can be seen that the

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13. Michelson, H. E.: Pemphigus Vulgaris, Showing Remission After Treatment with Germanin: Dermatitis Medicamentosa, Arch. Dermat. & Syph. **36**: 240 (July) 1937.

14. Becker, F. T., in discussion on Michelson.[13]

15. Wells, H. G.; Humphreys, E. M., and Work, E. G.: Significance of the Increased Frequency of Selected Cortical Necrosis of Adrenal as a Cause of Addison's Disease, J. A. M. A. **109**:490 (Aug. 14) 1937.

16. Vámos, L., and Böhm, S.: Arch. f. Dermat. u. Syph. **175**:174 (Feb.) 1937.

17. Dennie, C.: Personal communication to the authors.

18. Kinnear, J.: Brit. J. Dermat. **50**:236 (May) 1938.

drug has been in some hands and in some cases decidedly of value and in others of no value and even harmful through its toxic effects. We were especially impressed by the report of Tobias [6] and, having had occasion to treat 3 children with germanin in the past year, we consider our results worthy of recording. At the time when arrangements to report these 3 cases were being made it seemed that our clinical results from germanin therapy could be regarded as excellent. Since then, however, 1 patient has died, and we wish to present these 3 cases and the results which followed germanin therapy in a thoroughly unprejudiced manner.

REPORT OF CASES

CASE 1.—D. F., an American girl aged 6 years, was first seen on April 23, 1937, because of a generalized vesicular eruption. Three months prior to our observation of this patient, she had taken syrup of ferrous iodide in 12 drop doses three times daily for four days for the relief of a recurrent infection of the upper part of the respiratory tract. Shortly thereafter a widely distributed vesiculobullous eruption developed and spread to include the mouth. Although the iodide was discontinued within a week after the onset of the eruption, new lesions continued to form and individual ones became larger. The past and the family history were irrelevant.

Examination showed a well nourished and developed but tired-appearing girl of 6 years, with an eruption of discrete and confluent tense vesicles and bullae on the trunk, the arms and the legs and about the ears, tending to confluence about the neck and more thickly set over the lower part of the abdomen, the pubic region and the upper parts of the thighs (fig. 1). The lesions varied in size from that of a pea to that of a bean, were tense and thick walled and contained clear to seropurulent fluid. An occasional lesion was serosanguineous. None of the lesions presented an inflammatory base. Nikolsky's sign was absent. The tonsils were large and embedded. General examination showed no other abnormality.

It was felt that the patient had juvenile pemphigus, although diagnoses of erythema multiforme and dermatitis medicamentosa from iodides were considered. She was admitted to the hospital for study and treatment.

Course in the Hospital.—Urinalysis on admission showed no abnormality. The hemoglobin content was 80 per cent and there were 4,870,000 red blood cells and 15,600 white blood cells, with a differential count of 65 per cent polymorphonuclears, 31 per cent lymphocytes, 1 per cent monocytes and 3 per cent eosinophils. The rate of sedimentation of the red blood cells was 22 mm. in one hour. The Pels-Macht test showed toxicity (57 per cent). Repeated tests for iodides in the urine gave negative results.

The patient was put on a high vitamin, iodine-free diet and given 1 grain (0.065 Gm.) of iron cacodylate intravenously and 1.5 cc. of a blood-coagulating preparation intramuscularly on alternate days. Local treatment consisted of corn starch baths and the use of boric acid and starch powders. Some of the older lesions showed moderate healing, but many new vesicles and bullae continued to appear. After the patient had been in the hospital for one week scarlet fever developed. She was transferred to a hospital for patients with contagious disease for three weeks. The scarlet fever ran a typical, rather severe course without

complications or sequelae, but her pemphigoid eruption was greatly exacerbated, becoming almost universal during the last two weeks of her quarantine. During her illness with scarlet fever, administration of the iron cacodylate and the blood-coagulating preparation was continued, and four intramuscular injections of 20 cc. of blood and three intravenous transfusions of 200 cc. of citrated blood were given. After her recovery from scarlet fever she was readmitted to the Bishop Clarkson Memorial Hospital; she was somewhat cachectic, and her pemphigus was fully twice as extensive as at the time of her original admission. A high vitamin diet and administration of iron cacodylate and the blood coagulant were continued

Fig. 1 (case 1).—Juvenile pemphigus before germanin therapy.

and she was given 6 cc. of viosterol daily. High colonic irrigations were used daily for one week. There was no change in the eruption. Sulfanilamide was given four times daily in 10 grain (0.6 Gm.) doses for three days, when cyanosis developed and the medication was discontinued, no benefit from it being observed. Two more transfusions of 200 cc. of blood were given, with no apparent effect on the eruption. Fifty-five days after the original admission to the hospital all therapy except baths and application of boric acid ointment was discontinued.

Germanin was then given intravenously every other day for five injections, the doses being 0.2, 0.3, 0.4, 0.45 and 0.5 Gm. After the third injection it was apparent that all the lesions were beginning to heal. Ten hours after the fourth

injection the temperature rose to 102.6 F. and the pulse rate to 140. Twenty-four hours later the temperature was 102 F. and the pulse rate 120. Urinalysis showed no abnormality. Six hours after the fifth injection of germanin the temperature rose to 105 F., and the pulse rate was 100 and the respiratory rate 22; at this time a marked scarlatiniform erythema appeared, and the urine showed a trace of albumin and a few hyaline and granular casts. Within two days the fever and erythema subsided, and the urinary findings returned to normal. The eruption was entirely healed four days after the last injection of germanin. The patient has been well and strong since, and there has been no recurrence of the eruption. Ten weeks after the patient left the hospital, the Pels-Macht test showed a reading of 68 per cent. Figure 2 shows the condition of the patient's skin nine months after she left the hospital.

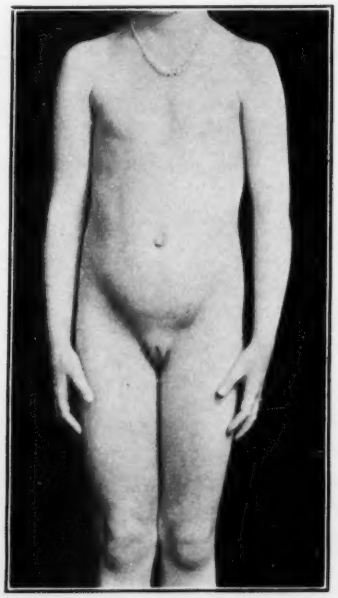

Fig. 2 (case 1).—Patient shown in figure 1 nine months after germanin therapy.

CASE 2.—J. J., an American boy aged 2½ years, was first seen by us on Aug. 4, 1937. A vesiculobullous eruption had developed five months before, appearing first on the face and neck and later on the lower part of the abdomen, the pubic and the genital region and the upper inner parts of the thighs. It had regressed slightly and exacerbated several times. The eruption had been treated as impetigo with silver nitrate and ammoniated mercury ointment, without benefit. Several roentgen treatments had been given prior to our observation. There had been no oral lesions. The general health had not been disturbed. There was no history of ingestion of iodide or any other drug. The family and the past history were irrelevant.

Examination showed a well developed and well nourished boy of 2½ years, not generally ill, with a vesiculobullous eruption under the chin, on the neck anteriorly and over the lower part of the abdomen, the pubic and the genital region

and the anterior and inner surfaces of the thighs. The lesions were tense and thin walled; their average size was that of a pea, and some had clear fluid contents, some seropurulent and a few sanguineous. There was no peripheral erythema. The coalescent areas showed some erosion and weeping where vesicles had ruptured. There were no oral lesions, and Nikolsky's sign was absent. General examination showed no abnormality except for the condition of the skin. A diagnosis of juvenile pemphigus was entertained, and the patient was hospitalized.

Course in Hospital.—Urinalysis showed a trace of albumin persistently, but no casts; there were some bacteria at times. There were 81 per cent hemoglobin, 4,840,000 red blood cells, and 14,000 white blood cells, with 63 per cent polymorphonuclears, 35 per cent lymphocytes, 1 per cent basophils and 1 per cent monocytes. The Wassermann reaction was negative. Examination of the stool showed no abnormality except a 1 plus reaction for occult blood. The Pels-Macht test of the serum at the time of admission showed toxity of 50 per cent.

During the first five days of hospitalization local treatment consisted of corn starch baths and application of dressings wet with boric acid. No internal medication was used. Many new vesicles and bullae continued to appear, and on the fifth day of hospitalization germanin therapy was instituted.

The drug was given intravenously, the first three injections every other day and the remaining three every third day, the doses being 0.2, 0.2, 0.2, 0.25, 0.3 and 0.3 Gm. There was no definite toxic response until the evening after the sixth injection, when the temperature rose to 103.2 F. (rectal) and there was slight general erythema. For another five days the rectal temperature in the evening was 101 F., returning to normal thereafter. The urine showed albumin (a trace to 2 plus) and casts (a few to 3 plus) for one month. (In the next three months there was no albumin, but an occasional cast was present.) Bacteria persisted in the urine in spite of the administration of various urinary antiseptics by mouth.

The cutaneous lesions healed slowly after the fifth injection of germanin but somewhat more rapidly after the sixth, being entirely healed in ten days. The nonprotein nitrogen content of the blood was 36.3 mg. per hundred cubic centimeters two weeks after the last injection of germanin; four weeks after the last treatment the blood pressure was 105 systolic and 60 diastolic. The patient was discharged from the hospital, apparently well, fifty-two days after admission. He had had no recurrence of his eruption and is in excellent health nine months after therapy.

CASE 3.—J. R., an American boy aged 10 years, first seen by us on Sept. 8, 1936, had had sores in his nose and mouth almost continuously for one year. During the past three weeks tender vesicopustules had developed on his feet and legs. There had been no disturbance of his general health. The past history was essentially normal. The family history was unimportant except that several persons on both the maternal and paternal side had had tuberculosis.

General examination, aside from that of the skin and of the oral and the nasal mucosa, showed no abnormality.

The eruption consisted of tense thick-walled vesicopustules ranging in size from that of a pea to that of a bean and was limited to the feet and legs. There was a definite tendency to patch formation, and many lesions had ruptured, leaving open oozing surfaces. Some patches showed central crusting surrounded by a peripheral zone of vesicopustules. Scattered over the oral mucosa were

erosions of irregular shape and size, some of them covered with a glistening white pellicle. The anterior nasal mucosa was covered with sanguineous crusts.

Course in Hospital.—On admission the oral temperature was 98 F., the pulse rate 78 and the respiratory rate 18. Urinalysis showed no abnormality. There were 90 per cent hemoglobin, 5,510,000 red blood cells and 9,800 white blood cells with a differential count of 68 per cent polymorphonuclears, 31 per cent lymphocytes and 1 per cent mononuclears.

Cultures of material from the nasal and oral lesions on Loeffler's medium showed no diphtheria bacilli. Repeated attempts to demonstrate fungi in material from both oral and cutaneous lesions were unsuccessful. Gram-positive cocci in pairs and long and short chains were found repeatedly in specimens taken from the nose and the mouth. No Vincent spirilla or fusiform bacilli were found. Staphylococcus aureus and pneumococci were cultured from material from the feet several times. No fungi were cultured from the feces on many trials.

During the first five months of hospitalization there were no significant changes in the patient's general condition except for the appearance of successive crops of patches of vesicopustules ranging in size from that of a pea to that of a bean in the pubic, the genital and the genitocrural area, about the face adjacent to the nose and lips and in the scalp and of an occasional discrete lesion on the extremities.

Ineffective Local Therapy: The following medicaments were used locally without effect during the first five months of hospitalization: on the skin, mercury bichloride (soaks and wet dressings), 0.25 per cent compound solution of iodine, methylrosaniline in various strengths, copper sulfate, black lotion, 10 per cent sodium thiosulfate and 4 per cent ammoniated mercury ointment; on the nasal and the oral mucosa, 40 per cent sodium borate in glycerin, sodium perborate, glyceryl borate, neoarsphenamine in glycerin, compound solution of sodium borate, methylrosaniline and carbolfuchsin. Baths of various types and fractional roentgen therapy were also found to be of no value.

General therapeutic measures found to be ineffective during the first five months included a high vitamin diet and administration of cod liver oil, of potassium iodide (10 grains [0.6 Gm.] three times a day), of antimony and potassium tartrate intravenously, of monilia vaccine intradermally in ascending doses, of a vitamin B preparation by mouth and of mixed typhoid vaccine intravenously in ascending doses.

During the fifth month of hospitalization it was decided to give colloidal iodine intravenously, potassium iodide by mouth having had no beneficial or harmful effect. Three daily injections were given, the first of 0.1 Gm. and the latter two of 0.2 Gm. Within a week the eruption became exacerbated and spread rapidly until 90 per cent of the surface of the body was covered with bullous lesions and oozing, bleeding denuded patches. Nikolsky's sign was demonstrable on the nonerupted skin. The mucosal lesions spread, coalesced and became more painful. The temperature ranged from normal to 103 F., the pulse rate from 100 to 140 and the respiratory rate from 20 to 30 per minute. The urine remained normal, but the blood count showed 77 per cent hemoglobin, 3,930,000 red blood cells and 15,200 white blood cells, with a differential count of 85 per cent polymorphonuclears, 10 per cent lymphocytes and 5 per cent eosinophils. The Pels-Macht test of the blood serum showed toxicity (57 per cent). The sodium chloride content of the blood was 475 mg. per hundred cubic centimeters. Blood cultures were negative.

For five weeks the patient was kept in a continuous tub bath at body temperature, a 1:6,000 solution of potassium permanganate, starch and weak tar, starch and boric acid and hypertonic saline solution being used at various times. Viosterol, calcium gluconate and a vitamin B preparation were given. One grain (0.065 Gm.) of iron cacodylate intravenously and 1.5 cc. of a blood-coagulating preparation intramuscularly were given on alternate days for two months. The patient received five blood transfusions (each of 250 cc. of whole blood). There was gradual healing of the more extensive bullous eruption, but the condition did not regress much beyond the point observed when the patient was first seen. High colonic irrigations were given, and sulfanilamide in 10 grain (0.6 Gm.) doses four times daily to the point of cyanosis and ½ grain (0.032 Gm.) of thyroid substance twice daily were administered without benefit. Exposures to sunlight resulted in no change.

After nine months' hospitalization without improvement, germanin therapy was decided on.

Effect of Germanin Therapy: Germanin was given intravenously every other day for five doses, the doses consisting of 0.2, 0.3, 0.4, 0.5 and 0.5 Gm. At the time the last dose was given, there was some indication of beginning healing of all lesions. Two days after the last dose of germanin the temperature rose to 100 F. for one day, and there was a slight toxic erythema for two days. The urine showed a trace of albumin but no casts the day after the last injection of germanin and was normal thereafter. A blood count at this time showed 109 per cent hemoglobin, 5,900,000 red blood cells and 8,600 white blood cells, with a differential count of 63 per cent polymorphonuclears, 32 per cent lymphocytes, 2 per cent monocytes and 3 per cent eosinophils. Ten days after the last dose of germanin the skin was entirely healed, and there were only a few small silvery membraneous pellicles in the mouth and the nose. The patient was discharged from the hospital.

Subsequent Course.—The lesions remained healed for two months, at the end of which time a few vesicopustules appeared about the toes and the soles. These were treated with tannic acid and silver nitrate (Bettman regimen), and wet dressings of 1:4,000 solution of potassium permanganate were used. The lesions healed, only to recur in another two months, at which time membranous erosions reappeared in the mouth. As the lesions failed to respond to the aforementioned local treatment, the patient was readmitted to the hospital for further study and care, five months having elapsed since his first course of germanin. The Pels-Macht test gave a result of 71 per cent (normal). The urine was normal; the nonprotein nitrogen content of the blood was 40 mg. per hundred cubic centimeters. The blood pressure was 120 systolic and 80 diastolic. A blood count showed 94 per cent hemoglobin, 5,180,000 red blood cells and 14,400 white blood cells, with a differential count of 70 per cent degenerated basophilic forms, 22 per cent polymorphonuclears and 8 per cent lymphocytes. A transfusion of 200 cc. of blood was given and in two days the blood count showed 97 per cent hemoglobin, 4,800,000 red blood cells and 8,000 white blood cells with a differential count of 62 per cent polymorphonuclears, 30 per cent lymphocytes, 2 per cent basophils and 6 per cent monocytes. The Kline test was negative. The only local therapy consisted of swabbing the mouth with sodium perborate and continuous application of dressings wet with boric acid to the feet.

Germanin was given on alternate days for five doses, of 0.3, 0.4, 0.5, 0.6 and 0.75 Gm., respectively. As there was no reaction and no apparent change in the lesions, three 1 Gm. doses were given at four day intervals. At this time the patient's temperature rose to 104 F., and there was a slight toxic erythema for

three days. The temperature continued to show a rise in the afternoon to from 100 to 103 F. during the following month. The urine remained normal. Healing of all cutaneous and mucosal lesions was complete in one week. The blood pressure fell to 85 systolic and 50 diastolic. The nonprotein nitrogen content of the blood rose at one time to 46 mg. per hundred cubic centimeters but fell to from 26 to 40 mg. The bleeding time was three minutes and the coagulation time two and three-fourths minutes.

At this time the patient was discharged to his home, 800 miles (1,290 kilometers) distant, and the material making up the remainder of this report was obtained through correspondence.

Fig. 3 (case 3).—Low power magnification of the adrenal gland, showing marked atrophy of the cortex.

His general condition improved and he felt well for one month. Two months after the last injection of germanin severe and protracted nausea and vomiting occurred and he was able to retain but little food or fluid. He became extremely prostrated and died ten weeks after the last injection of germanin. An autopsy was performed by Dr. A. T. Sudman, of Green River, Wyo., who furnished the following report of the gross picture:

"The body was that of a somewhat undernourished boy of about 12 years. The hair was thin and had a dry brittle appearance and feel. Except for a dry parchment-like appearance on the dorsum of the right foot, the skin appeared

normal. The right toe nails were absent. The left ones were short, dry and brittle.

"The mucosa of the nose, the mouth and the pharynx appeared normal.

"The heart was of normal size and was surrounded with the usual amount of clear pericardial fluid. The walls were of usual thickness, and the muscle appeared normal. The valves showed no thickening or calcification, and there were no evidences of endothelial change or intramural thrombi.

"The left lung was attached to the apex of the thorax by a thin adhesive band. In the lung, at the base of the adhesion, there was a small calcified area 1 cm. in diameter. In the left hilar region the tracheobronchial glands showed scattered areas of calcification. The remaining portion of the left lung and all of the right lung appeared normal.

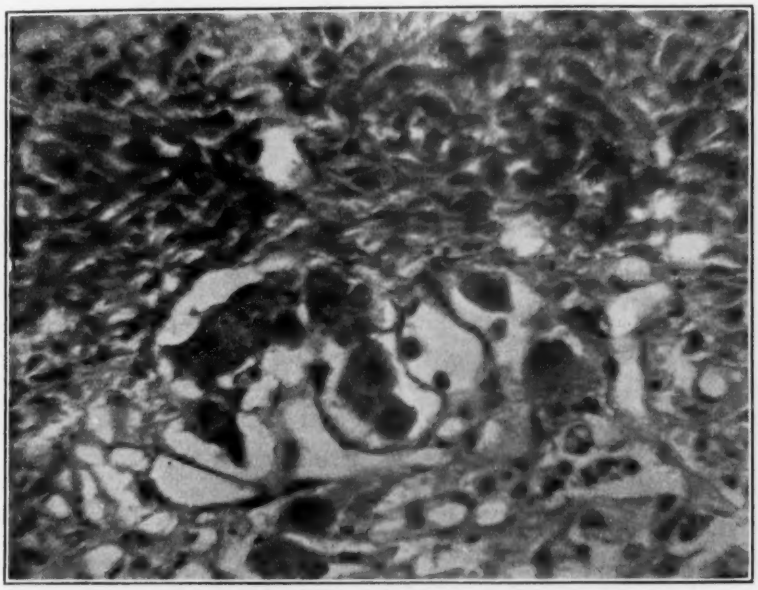

Fig. 4 (case 3).—High power magnification of the atrophic adrenal cortex, showing only a small nest of cortical cells.

"The abdominal cavity contained about 200 cc. of a clear amber-colored fluid. The mesenteric and the retroperitoneal lymph nodes were enlarged, some measuring 2 cm. in diameter.

"The mucosa of the stomach was moderately edematous and showed numerous scattered petechial spots. Similar changes were observed throughout the intestinal tract. There were no ulcerations.

"The liver was of normal size and appearance.

"The spleen was enlarged to three times the usual size but otherwise appeared normal.

"The pancreas showed no pathologic changes.

"The adrenal glands appeared somewhat smaller than normal and did not show the usual lipoid zone in the cortex. The kidneys were of normal size, and their cut surface presented nothing abnormal. The bladder was normal."

Histologic studies of representative specimens of tissue were made by Dr. Charles P. Baker, of Omaha.

"The skin was normal.

"In the stomach the gastric mucosa showed postmortem change of grade 2. Otherwise all layers were normal. An occasional small collection of mononuclear cells appeared in the muscle layers.

"The adipose connective tissue was normal.

"In the body of the pancreas acinar tissue appeared essentially normal, with islands of the usual appearance.

"The cardiac muscle showed some fragmentation, which was thought to have occurred post mortem. The cross striations in the muscle appeared normal. No collection of lymphocytes was noted.

"The spleen showed congestion (grade 2 plus) but was otherwise normal.

"In the kidney the glomeruli were normal except for moderate congestion. The tubules in the cortex appeared swollen and granular. Collections of mononuclear cells were scattered throughout, especially in the cortical region.

"The liver showed no evidence of fatty change. There was slight atrophy of the hepatic cords, with collections of lymphocytes scattered throughout.

"Examination of an abdominal lymph node showed the architecture to be well preserved. There was some stuffing of the sinuses with inflammatory cells. A chronic inflammatory reaction was present.

"The aorta was normal, with no arteriosclerosis.

"The lung showed congestion (grade 2 plus on a basis of 4). There were numerous heart failure cells, each containing considerable pigment judged to be blood pigment. There was edema of grade 2. Scattered throughout the sections of the lung collections of mononuclear cells appeared within the parenchyma, particularly in association with smaller bronchi. One calcified tubercle was present.

"In the small intestine postmortem change of grade 3 was the only abnormality.

"Several sections through both adrenal glands revealed that the cortex was almost entirely degenerated, with only an occasional nest of cortical cells remaining, sparsely distributed throughout the connective tissue framework of the organs" (figs. 3 and 4).

COMMENT

It is apparent that the type of lesions and their distribution in cases 1 and 2 were almost identical and could be regarded as belonging in the same category, which we have chosen to classify as "Juvenile Pemphigus." In these 2 cases the type of lesion, the distribution and the initial course were identical also with those in the case of Tobias.[8] Should one classify the condition as a juvenile type of dermatitis herpetiformis, the therapeutic response would correspond to that in Urbach's[19] (1932) case, in which a 4 year old child with dermatitis herpetiformis was successfully treated with germanin.

It will be noted that in cases 1 and 3 there was a history of ingestion of iodine. In case 1 three months had elapsed between the taking of syrup of ferrous iodide and hospitalization. The patient was then

19. Urbach, E.: Dermat. Wchnschr. **95**:1521 (Oct. 15) 1932.

placed on an iodine-free diet, and at no time were iodides found in the urine. We feel that these facts rule out a diagnosis of bullous iododerma. In case 3, although 10 grain (0.6 Gm.) doses of potassium iodide three times a day had no apparent influence, a generalized bullous eruption did develop after three intravenous injections of colloidal iodine. While we believe that iodine exacerbated this patient's pemphigoid state, there is no reason to believe that iodine was a factor at the time of the onset of the patient's illness.

Case 3 was the only one in which a second course of germanin was given. On the second admission to the hospital, the blood pressure, the urine, the nonprotein nitrogen and hemoglobin contents of the blood and the red blood cell and the total leukocyte count were normal. However, the differential count showed 70 per cent degenerated basophilic forms. Should this have been a warning sign? We did not believe so, especially as the differential count reverted to normal after a transfusion of 200 cc. of blood. In retrospect, it would seem that more consideration might have been given to the fall in blood pressure from 120 systolic and 80 diastolic to 85 systolic and 50 diastolic after a second course of germanin as suggesting an incipient addisonian syndrome. Unfortunately determinations of the potassium and the sodium content of the blood were not made; these might have pointed to the probability that atrophy of the adrenal cortex was occurring and have led us to consider treatment with extract of adrenal cortex and with sodium chloride. Case 3 is the second recorded case of atrophy of the adrenal cortex and death due to germanin, the first case having been reported by Wells, Humphreys and Work.[15]

Dosage and Manner of Use of Germanin.—In the administration of germanin the dose should be carefully chosen and adjusted to the tolerance of the individual patient. Adults may be given an initial dose of 0.5 Gm., with subsequent doses of 1 Gm. every other day for another four doses, providing toxic signs, such as albuminuria, fever and toxic erythema, do not appear. It is our opinion that no more than five intravenous injections at two day intervals should be given in one course.

While germanin is being administered, we recommend that daily urinalysis and daily determination of blood pressure be made; that frequent complete blood counts be done; that the nonprotein nitrogen content of the blood be determined frequently, and that determinations of the potassium, the sodium and the chloride content of the blood be made, in order that degeneration of the adrenal cortex may be detected early.

SUMMARY AND CONCLUSIONS

The literature on germanin in the treatment of pemphigus is reviewed.

Two apparent cures of juvenile pemphigus with germanin are reported.

One fatality from germanin therapy is reported, death being due to atrophy of the adrenal cortex.

Patients receiving germanin therapy should be studied from the standpoint of renal and hemopoietic function and the function of the adrenal cortex watched. The blood pressure and the potassium, the sodium and the chloride content of the blood should be ascertained frequently.

IS LICHEN NITIDUS A VARIETY OF LICHEN PLANUS?

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Haynes and Hellier [1] recently reported a case of lichen planus associated with lichen planus hypertrophicus, lichen planus acuminatus (spinulosus) and lichen nitidus. Histologic examination of lesions of the last two diseases showed an infiltration characteristic of the last condition, consisting of epithelioid cells, lymphocytes and giant cells. The authors stated that the observation of these various associated lesions suggested *"une parenté étroite"* between lichen nitidus and lichen planus. We decry with Haynes [2] the lack of agreement on the terminology of the variants of lichen planus. He called the acuminate lesion lichen verrucosus, but the latter never shows the histologic [3] picture of lichen planus. Cases of associated lichen planus and lichen nitidus had been previously reported by Civatte,[4] Rabut and Guex [5] and Barber.[6] Juliusberg [7] discussed cases of a similar association. Pels [8] published the report of an interesting case of miliary lichen planus in which there were areas of infiltrate similar to those observed in cases of typical lichen nitidus.

From the Johns Hopkins Medical School, Department of Dermatology.

1. Haynes, H., and Hellier, F.: Lichen nitidus associé à du lichen plan et à de la lichénification verruqueuse, Ann. de dermat. et syph. **8**:192, 1937.

2. Haynes, H.: Personal communication to the authors.

3. McCarthy, L.: Lichen Ruber Verrucosus, in Histopathology of Skin Diseases, St. Louis, C. V. Mosby Company, 1931, p. 219.

4. Civatte, M.: Lichen nitidus coexistant avec un lichen plan, Bull. Soc. franç. de dermat. et syph. **22**:65, 1911; "Lichen nitidus" et lichen plan, ibid. **34**: 667, 1927.

5. Rabut and Guex: Lichen ruber et lichen nitidus associés, Bull. Soc. franç. de dermat. et syph. **36**:261, 1929.

6. Barber, H. W.: Confluent Lichen Nitidus with Lesions on the Tongue, Proc. Roy. Soc. Med. **20**:1052, 1927; in discussion on Sibley, K.: Lichen Nitidus, Brit. J. Dermat. **43**:138, 1931.

7. Juliusberg, F., in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 128.

8. Pels, J. R.: A Case of Miliary Lichen Planus with Unusual Clinical and Pathologic Findings, J. Cutan. Dis. **32**:821, 1914.

Since Haynes and Hellier's publication, Lewis [9] reported a case of lichen planus with lichen nitidus in which the histologic pictures were typical of each type of lesion. Traub [10] in January 1937 presented a case of lichen planus and lichen nitidus, but no biopsies were made. In the discussion he mentioned that a colleague had a similar case in which the histologic picture was typical of the two conditions. Rasykes [11] reported 2 cases of the two diseases. Each showed typical histologic pictures.

If one attempts to support the fortuitous association of lichen planus and lichen nitidus from a statistical point of view, one is impressed by the sparsity of figures on the frequency of occurrence of the latter disease; for example, in the statistical report of the American Dermatological Association for 1916,[12] there were 58,387 cases of cutaneous disease, of which 404 (0.691 per cent) were of lichen planus; no cases of lichen nitidus were noted. Hazen [13] in 1935 made a statistical report on 11,729 cases of cutaneous disease in the Negro (excluding cutaneous syphilis); there were 34 cases (0.29 per cent) of lichen planus and 4 cases (0.034 per cent) of lichen nitidus.

In 1937 2 patients with both types of lesions were seen in the Johns Hopkins dermatologic clinic.

REPORT OF CASES

CASE 1.—L. K., a white woman aged 21, was first seen on April 30, 1937, because of a generalized eruption. Her past history was essentially irrelevant except for a "nervous breakdown" during the preceding summer. Examination showed three distinct types of cutaneous lesions. On the flexural surfaces of the wrists, the elbows and the knees there were discrete and confluent violaceous flat angulated shiny papules from 2 to 5 mm. in diameter, with umbilicated centers. Some of the papules had an annular arrangement. Typical lesions of lichen planus of the acuminate type were seen on the flexural surfaces of the forearms and the elbows and on the anterior parts of the thighs. These were composed of variously sized groups of minute discrete acuminate keratotic follicular papules which gave the skin the feel of a nutmeg grater.

On the less involved area of the extensor surfaces of the thighs there were discrete skin-colored angular nonscaly flat papules 1 or 2 mm. in diameter; some of these had slightly depressed centers. No lesions were seen on the vulva or on the mucous membranes.

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9. Lewis, G. M.: Lichen Nitidus and Lichen Planus: Case Report, Arch. Dermat. & Syph. **36**:436 (Aug.) 1937.

10. Traub, E. F.: Lichen Planus and Lichen Nitidus, Arch. Dermat. & Syph. **36**:895 (Oct.) 1937.

11. Rasykes, B.: Lichen Nitidus, in Wise, F., and Sulzberger, M.: The Year Book of Dermatology and Syphilology, Chicago, Year Book Publishers, Inc., 1934, p. 356.

12. Pollitzer, S.: Statistical Report of the American Dermatological Association for the Year 1916, J. Cutan. Dis. **36**:294, 1918.

13. Hazen, H. H.: Syphilis and Skin Diseases in the American Negro, Arch. Dermat. & Syph. **31**:316 (March) 1935.

The general physical examination showed no essential abnormality. No clinical evidence of tuberculosis was found, but the intracutaneous test with old tuberculin with a 1:1,000 dilution (0.1 mg.) resulted in an area of erythema about 2 cm. in diameter and a central papule of 1 cm. Other laboratory tests showed nothing abnormal except mild secondary anemia. The basal metabolic rate was —8 per cent.

Clinically the patient had lichen planus, lichen planus acuminatus and lichen nitidus.

Histologic Observations.—A section from a typical area of lichen planus showed moderate hyperkeratosis with slight patchy parakeratosis, some uneven acanthosis and shallow keratotic plugging. Slight evidence of edema was seen in the sub-

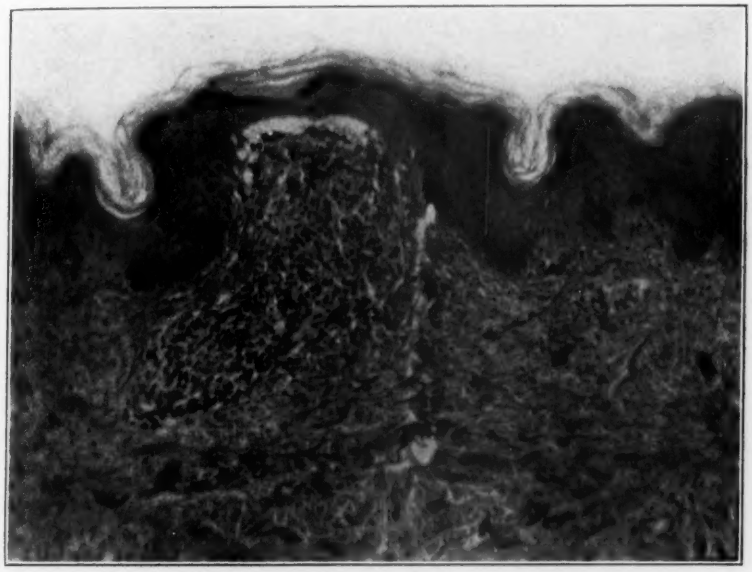

Fig. 1 (case 1).—Papule of lichen nitidus showing single giant cell.

epidermal layer of the cutis. High in the cutis the infiltrate was well defined and consisted of lymphocytes and epithelioid cells, which extended slightly into the deeper cells of the rete.

The second biopsy specimen was from a discrete small skin-colored papule. The area of infiltration was about the width of three pegs. The epidermis was atrophic, with a narrow cleft between the epidermis and the infiltrate, which was confined mostly to the papillary layer and was composed of lymphocytes and epithelioid cells and an occasional giant cell. There was no necrosis. Elsewhere in the cutis there was a mild perivascular infiltrate.

The third biopsy specimen was taken from an area containing minute keratotic papules and lichen-nitidus-like lesions. The latter showed a picture similar to that seen in the slides of the second specimen, except that the edema in the infiltrated area was more pronounced. The former lesions, which were composed of keratotic follicular plugs, extended deeply into the cutis. The infiltrate about these keratotic lesions consisted mostly of lymphocytes and epithelioid cells and

was most marked at the upper and the lower third of the keratotic plugs. No giant cells or necrosis was present. The histologic diagnoses made were lichen planus, lichen nitidus and lichen planus acuminatus (spinulosus).

CASE 2.—B. P., a white woman aged 35, was first seen in the dermatologic clinic on Nov. 22, 1937, because of a generalized pruritic eruption. In 1933 she had suffered from postpartum parametritis, with thrombophlebitis of the pelvic veins and pulmonary infarcts. At that time she had mild secondary anemia. Her Wassermann reaction was negative, and she had a basal metabolic rate of + 4 per cent.

The eruption, which had been present for two months, was on the flexural surfaces of the forearms, the elbows, the wrists and the inner surfaces of the

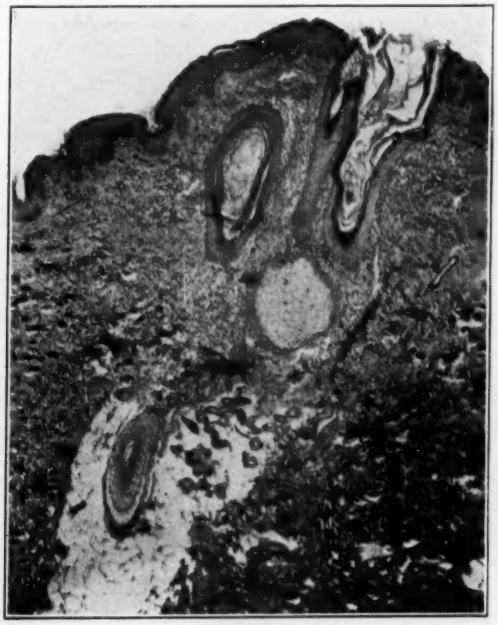

Fig. 2 (case 1).—Lesion of lichen planus spinulosus from the same biopsy specimen as the section in figure 1.

thighs, the upper part of the chest and the abdomen. It consisted of small papular angulated slightly scaly lesions. Some of the papules on the wrists were shiny and umbilicated, and others were in the lines of scratch marks (Koebner reaction). Two biopsies were made.

Histologic Examination.—The first biopsy specimen was made from a lichen-nitidus-like lesion on the side of the abdomen. The epidermis was slightly atrophic but was even thinner over the areas of infiltration than elsewhere. These areas were moderately well defined, but only a few showed any tendency to limitation to interpapillary spaces, where the cells were loosely packed. There were epithelioid cells and lymphocytes, extending up to the basal layer. Deeper in the cutis there was some perivascular infiltration of the subacute type.

The second section was from a lesion on the forearm, which showed a Koebner reaction. There were slight hyperkeratosis, moderate acanthosis and a well

defined infiltration, which consisted mostly of mononuclear leukocytes and an occasional epithelioid cell. The infiltrate extended slightly into the lower layer of the rete. The rest of the cutis showed a mild perivascular collection of cells. The histologic diagnoses were lichen nitidus and lichen planus.

In our files of histologic examinations for the past ten years we have records of 101 cases of lichen planus and of 13 cases of lichen nitidus. Those of the latter group have been obtained since 1934. In looking over the slides of lichen planus, we found 3 cases in which, besides typical lichen planus, there was a lichen-nitidus-like papule in some part of the section; in 1 there was a picture of atypical lichen nitidus while in still another there was a lesion which could be interpreted as a large lichen-nitidus-like pale papule or a small lichen planus papule.

SUMMARY

In the recent literature the number of reports of lichen nitidus associated with lichen planus is increasing. Two more cases are reported, and a review of our microscopic sections suggests that histologically the two types of lesions are more often associated than has been suspected. We feel that Haynes and Hellier were correct in considering that there is a close relation between the two diseases. Seven per cent of our histologic sections of lichen planus showed a lichen-nitidus-like lesion.

MELANOTIC SARCOMA WITH EXTREME MELANOSIS

REPORT OF A CASE

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A case of melanotic sarcoma with widespread metastases involving all tissues, including the brain and the spinal cord, recently came under my observation. In view of the rarity of this disease with such widespread metastases, a report of the clinical and pathologic observations in my case may be of interest.

REPORT OF CASE

G. S., a well developed man aged 70, a cooper, reported to the dermatologic clinic of the Toronto General Hospital in April 1936. A dark brown mole had been present in the right axilla for thirty-five years. About one year prior to his visit to the hospital the lesion began to enlarge, became irritable and bled when rubbed. Apart from the mole the only complaint was of fatigue. Examination showed a raised hard purplish black mole in the right axilla, 2 cm. in diameter; immediately about the margin were smaller, elevated hard black nodules. Similar pigmented lesions were present in the cheeks, the scalp and the scapular areas. All were stony hard and apparently unattached to deeper structures. A biopsy specimen was removed from the primary lesion in the right axilla and another from a nodule on the cheek. The specimen from the primary lesion showed two rounded, fairly well circumscribed, darkly pigmented areas. These areas were not encapsulated. The specimen from the face showed an elevated, darkly pigmented nodular mass. Microscopically the specimens were similar. The corium was occupied by a large, poorly defined nodular mass made up of small groups of polyhedral or spindle cells. These cells were rather large, with pale-staining vesicular nuclei, and many of them were crowded with granules of brown pigment. There was considerable variation in the size of the cells, and an occasional mitotic figure was identified. The pathologic diagnosis was melanotic sarcoma.

Palliative treatment was prescribed, and the patient was requested to report to the clinic at intervals for observation. He did not return to the clinic and in the interim received some roentgen treatment and injections of a so-called "cancer cure" without apparent effect.

In October 1936 the patient began to complain of more marked fatigue, dizziness, nausea, headache, failing vision and numbness in the left hand. One week before death, in January 1937, he reported for admission to the Toronto General Hospital.

From the Department of Medicine, University of Toronto, and the Medical Service, Toronto General Hospital.

Read at the Sixty-First Annual Meeting of the American Dermatological Association, Inc., Del Monte, Calif., June 9, 1938.

Physical Examination.—The skin generally was deeply pigmented and especially so underneath the arms, over the nipples and about the genitalia. The entire cutaneous surface from scalp to soles was covered by nodules and nodes, ranging from one the size of a pinhead to one 4 by 2.5 cm., which was just above the left nipple. Most of the lesions were slightly raised above the skin and were round or oval. They were all a uniform dark brown, and no nodules could be found which were not pigmented. The nodules were most numerous on the face and scalp, gradually decreasing in number over the body surface, and were

Fig. 1.—Photograph taken Aug. 29, 1936.

less numerous on the lower parts of the legs and the forearms; they were practically absent on the palmar and plantar surfaces and on the glans penis. Those on the face formed a confluent mass, and little cutaneous surface was present which was not involved. The skin about the eyes and over the left side of the nose showed numerous erupted areas with crusts of dried pus. The eyelids could be opened only slightly. There were marked conjunctivitis in both eyes and tumorous invasion of the right sclera. The nares were practically obliterated, owing to the extensive involvement of the skin about these orifices. The right axilla, the site of the primary lesion, presented a crusted mass of nodular tissue measuring 10 by 15 cm. This mass had the consistency of leather; in several places bleeding had occurred. The tissues immediately surrounding the mass

were studded with numerous molelike tumors. Small nodules were present in the skin of the penis, the scrotum and the testes. The inguinal glands were extensively involved.

The liver was palpable below the right costal margin. It was tender, but nodularity could not be determined because of the nodules in the skin.

There were small, dark purplish nodules on the gums, the hard palate and the tongue.

Fig. 2.—Photograph taken Nov. 30, 1936.

Reflexes were diminished, except that of the brachioradialis muscle, which was normal. Sensitivity to light touch, to temperature and to pinprick were within normal limits.

Laboratory Examination.—The urine was light brown and acid; the specific gravity was 1.015; there was a trace of albumin but no sugar; the ferric chloride test for melanin gave a strongly positive result. Microscopic examination showed occasional red blood cells, little hyalin and granular casts.

Examination of the blood showed 93 per cent hemoglobin, 4,970,000 red blood cells and 9,600 white blood cells. The red blood cells showed moderate anisocytosis and some polychromasia. Blood culture and the Wassermann test were negative. A determination of nonprotein nitrogen showed 70 mg. per hundred cubic centimeters.

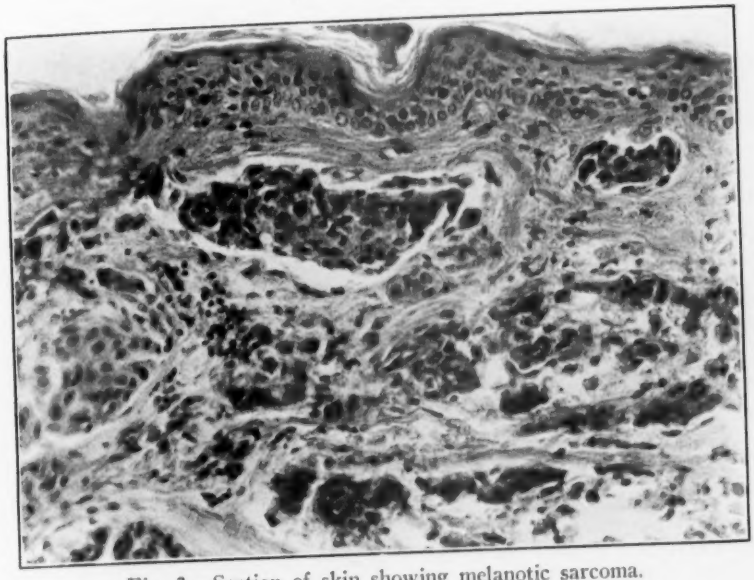

Fig. 3.—Section of skin showing melanotic sarcoma.

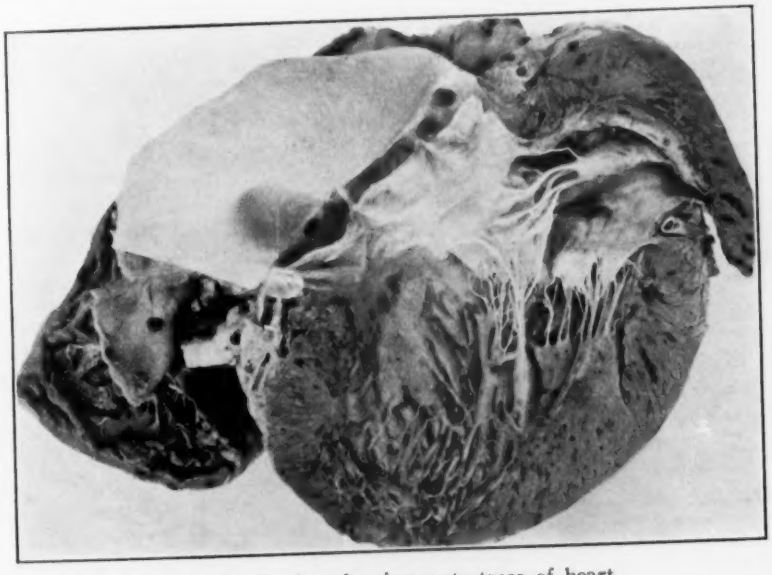

Fig. 4.—Section showing metastases of heart.

Autopsy.—The following is a summary of the observations made at autopsy by Dr. G. Lyman Duff: (The lesions seen at autopsy were confined almost exclusively to the widespread pigmented metastases. Apart from the presence of tumor nodules, all the organs were essentially normal except the heart, which was moderately hypertrophied but had no valvular lesions.)

Incisions through the thoracic and the abdominal wall revealed numerous dark brown nodules in the subcutaneous tissues. Other small pigmented nodules were sparsely scattered in the voluntary muscles of the thorax and the abdomen. The peritoneal, pleural and pericardial fluid was dark brown.

The cut surface of the thyroid gland showed numerous pigmented nodules varying from minute dots to lesions 5 mm. in diameter.

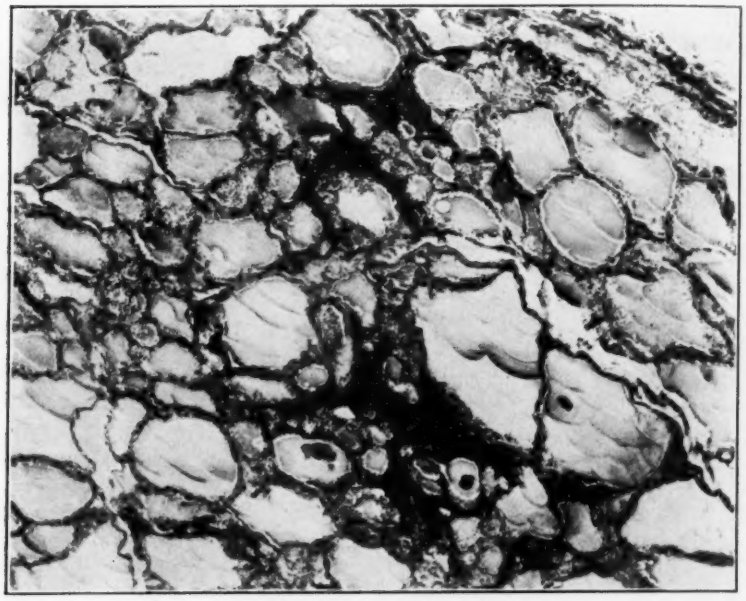

Fig. 5.—Section showing metastases in thyroid.

The epicardial surface of the heart was everywhere studded with firm, dark brown tumor metastases varying from minute size up to about 5 mm. in diameter. The endocardium was similarly affected, the nodules being most abundant in the right auricle and in the region of the ring of the mitral valve. The cut surfaces of the myocardium were peppered with small, slightly elongated dark patches which lay with the long axis parallel to the direction of the muscle fibers. Most of these patches were not more than 2 or 3 mm. wide.

The pleural surfaces of both lungs were closely studded with small brown tumor nodules, and similar small masses of tumor were numerous in the peribronchial lymph nodes; no metastases were visible in the parenchyma of the lungs.

The spleen showed numerous brown nodules scattered over the capsular surface, and serial slices revealed four brown pigmented patches in the pulp. The smallest of these measured 4 mm. in diameter.

Numerous cut surfaces of the pancreas showed brownish streaks and small brown patches in the interlobular connective tissue and fat.

The liver was enlarged by the presence of numerous metastases. These were scattered everywhere just beneath the capsular surface and throughout the whole hepatic substance. Seen on the cut surface, they varied from dots the size of a pinhead to rosette-shaped or lobulated masses which measured up to 5 cm. in greatest diameter. The wall of the gallbladder was occupied by many small pigmented metastases, which were visible from both the inner and the outer surface.

The esophagus was surrounded by numerous small tumor nodules lying in its outer coats.

The serous surfaces of the stomach presented only a few scattered brown nodules, but throughout the small and the large intestine such rounded masses were numerous, especially in the small intestine along the line of the mesenteric attachment, where they reached a diameter of 1 cm.

The mucous surface of the esophagus was free from nodules, but the mucosa of the stomach, the duodenum, the small and the large intestines and the rectum presented scattered small dark brown, elevated areas. The large intestine was somewhat less involved than was the small bowel. At no point was there any ulceration of the mucosa overlying the nodules.

Both adrenal glands contained scattered minute brown islands of tumor tissue. Both kidneys were peppered with minute metastatic tumors, which were even more numerous in the walls of the renal pelves.

Similar small brown nodules were scattered over the mucous surfaces of the ureters throughout their entire length. The urine contained in the bladder was dark brown. The entire thickness of the wall of the bladder, including the mucosa, was studded with numerous small brown metastatic masses, but there was no ulceration. The mucosa of the urethra presented a few minute brown nodules.

Transverse slices through the prostate revealed only a single small brown metastatic tumor. Both testes and epididymes were occupied by numerous minute nodules.

The outer surface of the aorta with its surrounding connective tissue showed numerous small metastatic nodules throughout its length. Most of the retroperitoneal and mesenteric lymph nodes were slightly enlarged and contained small masses of tumor tissue.

A sample of bone marrow from the middle of the shaft of the right femur contained a few dark brown patches of metastatic tumor tissue.

The vault of the cranium, just beneath the periosteum, presented many small brown metastatic nodules. In the dura mater numerous dark nodules were scattered here and there, apparently incorporated in the membrane. These measured 2 or 3 mm. in diameter. Many small metastatic tumors were present in the leptomeninges and the underlying cerebral cortex, over the convexities of both cerebral hemispheres, the inferior surface of the left temporal lobe and the inferior surface of the left cerebellar hemisphere. A single, well defined nodule in the leptomeninges covered the right olfactory bulb. A horizontal section through the cerebral hemispheres at the level of the basal ganglions revealed numerous brown tumor nodules from 3 to 5 mm. in diameter. The majority of these occupied cortical tissue and subcortical white matter. The cavities of the lateral ventricles contained yellowish brown granular pigment. A sagittal section through the brain stem showed a well defined tumor nodule in the genu of the corpus callosum, but no metastases were visible in the brain stem. Numerous sections through the cerebellar hemisphere and the pons showed a few

minute brown areas of metastatic tumor tissue. The dura mater of the spinal cord contained numerous small brown nodules, and a few similar masses were seen in the leptomeninges, but multiple transverse sections failed to reveal any metastases in the cord itself. The cerebrospinal fluid was dark brown and contained peculiar brown gritty material resembling sand.

Examination of the numerous microscopic sections taken from the various organs confirmed the distribution of the metastases observed grossly, but many minute nests of tumor cells which could not have been visible to the naked eye were present in almost all the affected organs. Sections of the lungs which had presented no grossly visible nodules were likewise free from microscopic metastases. Sections of the left eye, however, which had shown no gross tumor, revealed a microscopic nest of melanotic tumor cells in the choroid.

The histologic character of the melanotic metastases was essentially the same in all locations. The tumor nodules consisted of small or large clusters of cells varying from polyhedral to spindle shape. The polyhedral shapes were observed most frequently where the cells occurred in solid masses, while the spindle shapes were found especially around the margins of the nodules, where tumor cells were infiltrating the neighboring tissues, or in places where only a few cells were to be seen lying crowded into tissue spaces. The nuclei of the cells were vesicular, large and round or oval. They varied greatly in size, shape and depth of staining, but mitotic figures were few.

The cells possessed an abundant, pink-staining cytoplasm which in practically every cell was more or less densely packed with finely granular brown melanin pigment. No islands of nonpigmented cells were present anywhere. The tumor cells infiltrated freely into surrounding tissues in all organs except the brain, in which the clusters of tumor cells were fairly well circumscribed. Even here, however, they could be seen in places extending into the adjacent zone of compressed brain tissue.

In the kidneys many glomeruli were occupied by small nests of tumor cells, and many of the tubules contained dark brown melanin casts. Large numbers of reticuloendothelial cells in the liver, the spleen and the lymph nodes were filled with granules of melanin pigment.

COMMENT

The theories regarding the origin of melanoma are well known. Dawson [1] expressed the apparent belief that the melanotic tumor cell arose in the endothelium from any endothelial cells of the cutis. Today I believe that Masson's [2] theory, viz.: that the nevus cell is derived from and belongs to the end organ of the peripheral sensory nerve, is generally accepted. Virchow [3] reported the first case of melanotic sarcoma of the arachnoid and attributed its origin to the chromatophores of the leptomeninges. In no place did the neoplasm penetrate the substance of the brain and the spinal cord.

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1. Dawson, J. W.: The Melanomata: Their Morphology and Histogenesis, Edinburgh M. J. **32**:501, 1925.

2. Masson, P.: Les naevi pigmentoire tumeurs nerveuses, Ann. d'anat. path. **3**:417, 1926.

3. Virchow, R.: Pigment und diffuse Melanose der Arachnoidea, Virchows Arch. f. path. Anat. **16**:180, 1859.

Apparently the disease may occur at any age. Berblinger [4] reported the case of a girl aged 9 months in whom multiple pigmented nevi were scattered over the body at birth. Death occurred from congenital hydrocephalus. Postmortem examination showed sarcomatosis of the brain and the meninges. My patient was 70 years of age. A pigmented mole had been present in the right axilla for thirty-five years.

Ewing [5] and Butterworth and Klauder [6] found the duration of the generalized disease to be about three years. My patient died eighteen months after the first sign of growth in the primary lesion.

The melanosis, though extreme in my case, giving a curious gun metal or argyria-like color to the whole surface of the body, was not so marked as in the case recently described by Odel, Montgomery and Horton.[7]

Globus and Selinsky,[8] reporting 12 cases of metastatic tumor of the brain, referred to the lack of objective neurologic signs. In my patient signs of intracranial pressure, viz. headache, dizziness, nausea and faulty vision, occurred about three months before death.

Wortis and Wortis,[9] reviewing the records of Bellevue Hospital, found 6 cases of melanoma with metastases involving the central nervous system. The chief complaint was severe headache. In Netherton's [10] case of extensive pigmented nevus with primary melanoblastosis of the leptomeninges the patient was well until seven weeks prior to admission to the hospital. The complaints were headache, blurring vision and loss of memory.

Globus and Selinsky [8] found that secondary malignant tumor of the brain substance spares the cranila bone. My experience was similar, though the dura and the periosteum were extensively involved.

Wortis and Wortis [9] demonstrated melanin in the spinal fluid in 1 case and in the urine in 4 of their 6 cases. In 4 of their cases metastases were found in the heart. In my patient the urine contained melanin,

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4. Berblinger, W.: Ein Beitrag zur epithelialen Genese des Melanins, Virchows Arch. f. path. Anat. **219**:328, 1915.

5. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1919.

6. Butterworth, T., and Klauder, J. V.: Malignant Melanomas Arising in Moles: Report of Fifty Cases, J. A. M. A. **102**:739 (March 10) 1934.

7. Odel, H. M.; Montgomery, H., and Horton, B. T.: Diffuse Melanosis Secondary to Malignant Melanoma, Proc. Staff Meet., Mayo Clin. **12**:742, 1937.

8. Globus, J. H., and Selinsky, H.: Metastatic Tumor of the Brain: A Clinical Study of Twelve Cases with Necropsy, Arch. Neurol. & Psychiat. **17**:481 (April) 1927.

9. Wortis, H., and Wortis, S. B.: Metastatic Melanoma Involving the Central Nervous System, Arch. Neurol. & Psychiat. **36**:601 (Sept.) 1936.

10. Netherton, E. W.: Extensive Pigmented Nevus Associated with Primary Melanoblastosis of Leptomeninges of Brain and Spinal Cord: Report of a Case, Arch. Dermat. & Syph. **33**:238 (Feb.) 1936.

and the spinal fluid at autopsy, though not tested for melanin, was dark brown and contained brown, gritty, sandlike material. The cardiac valves were free of metastases, though the endocardium was extensively involved.

Early surgical removal of pigmented nevi subject to trauma was stressed by Farrell,[11] Handley [12] and McClure.[13] However, trauma is not necessary for development of melanoma. Williams and Martin,[14] reporting 25 cases of melanoma, found a history of trauma in only 1 case. My patient had no history of injury, unless one considers the movement of the arm over the axilla as irritating.

SUMMARY AND CONCLUSIONS

The case of a man aged 70 with melanotic sarcoma and extreme melanosis is reported. Death occurred eighteen months after the first evidence of change in a pigmented nevus in the right axilla. The skin was massively involved from head to foot, with the exception of the palms, the soles and the glans penis, where the nodules were few.

The earliest complaint was weakness. Evidence of intracranial pressure and marked loss of weight appeared about three months before death.

Primary malignant tumor of the brain differs from the lesion reported here by the presence of more definite neurologic signs.

The urine showed evidence of melanin.

The spinal fluid at autopsy was dark brown and contained brown, gritty, sandlike material.

Autopsy revealed melanotic sarcomatous deposits in all tissues, including the brain and the spinal cord.

A microscopic nest of melanotic tumor cells was present in the left choroid.

The parenchyma of the lung, the cardiac valves and the cranial bone were free of metastases, though the pleural surfaces, the endocardium, the dura and the periosteum were extensively involved.

Prof. Duncan Graham and Prof. E. J. Trow, physician in charge of dermatology, granted me permission to report this case. Prof. G. Lyman Duff furnished the pathologic report.

The discussion has not yet been received. It will be incorporated in the report of the meeting of the American Dermatological Association, in a later issue of the ARCHIVES.

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11. Farrell, H. J.: Cutaneous Melanomas, with Special Reference to Prognosis, Arch. Dermat. & Syph. **26**:110 (July) 1932.

12. Handley, S.: Prognosis of Simple Moles and Melanotic Sarcoma, Lancet **1**:1401, 1935.

13. McClure, J.: Melanotic Sarcoma: Survival Fourteen Years After Primary Operation, Lancet **2**:371, 1936.

14. Williams, I. G., and Martin, L. C.: Naevocarcinoma of the Skin and Mucous Membrane, Lancet **1**:135, 1937.

PSORIASIS OF THE NAILS

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Ungual lesions of psoriasis occur often enough to be worthy of serious consideration. When the process as a whole ceases to progress and no new ungual damage appears, an average minimum of one hundred and twenty days is still required for existing blemishes to grow out and be cut off. Ungual changes are among the most conspicuous of conditions affecting the cutaneous appendages and may be of great aid in the diagnosis of psoriasis. One of the most notable features of psoriatic nails observed in the series of cases to be reported has been the changes in color, which will be emphasized later.

LITERATURE

One of the most interesting early references to psoriatic ungual changes appeared in Willan's [1] treatise on cutaneous diseases in 1809:

> The Psoriasis Unguium sometimes occurs alone, but it is usually connected with scaly patches on the arms, hands, etc. In some cases, the nails from the middle appear brown or yellowish; they bend upwards and are ragged at the ends and rough on the surface. In other cases, they are thickened, deeply indented, and bent downward over the ends of the fingers.

A fair amount has been written on this subject since, with perhaps little addition to this description by an early master.

An excellent monograph was published in 1900 by Heller,[2] who estimated the incidence of ungual changes in psoriasis at 10 per cent. He stated that pitting over dilated capillaries was the earliest change and called other lesions late forms. He mentioned opacity of the nail plate but no specific variations in color.

In 1902, White [3] reported a study of 485 cases of ungual disease, including 67 instances of psoriasis. The commonest lesions were those associated with hyperkeratosis of the nail bed, e. g., yellow to dark brown discoloration; transverse depressions; increased convexity with granular detritus under the nail plate; exfoliation of surface cells with

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From the Department of Dermatology and Syphilology of the Massachusetts General Hospital, C. Guy Lane, M.D., Chief.

1. Willan, R.: Cutaneous Diseases, Philadelphia, Kimber & Conrad, 1809.
2. Heller, J.: Die Krankheiten der Nägel, Berlin, A. Hirschwald, 1900.
3. White, C. J.: The Clinical Study of Four Hundred and Eighty-Five Cases of Nail Disease, Boston M. & S. J. **147**:537 (Nov. 13) 1902.

thinning, and increased brittleness with or without leukonychia. Pitting was, of course, present.

Dubreuilh [4] in 1904 gave the incidence of ungual lesions in psoriasis as from 10 to 20 per cent. Changes were described as cup-shaped depressions, diffuse or local modifications of color from reddish brown to smoky yellow, furrows, grooves, crumbling and desquamation. The statement was made that none of these changes was specific for psoriasis.

Nägeli [5] in 1935 stated that 10 per cent of patients with psoriasis had ungual changes. The lesions mentioned by other writers were adequately described and were separated into primary lesions of the nail plate and those secondary to changes in the matrix, the nail bed and the adjacent tissues. Loss of transparency was listed as a diffuse primary change. Round yellow spots were attributed to psoriatic lesions in the matrix and classed as secondary phenomena. No other anomaly of color wes mentioned.

In Pardo-Castello's [6] comprehensive monograph on ungual diseases, published in 1936, the author stated that psoriatic nails comprised 5.38 per cent of all ungual lesions in his experience and had been present in 15 per cent of his cases of psoriasis. The ungual changes observed in psoriasis were well described, although variations in color received little emphasis; a loss of luster, a whitish appearance of the plate and a yellowish mass beneath the plate were the only variations of this kind mentioned. The feeling that the ungual changes in psoriasis are not characteristic, expressed by other observers, was likewise expressed by Pardo-Castello. Eczema, psoriasis, dermatitis exfoliativa and ichthyosis were said to affect the nails in a similar manner, with the diagnosis resting on the recognition of concomitant cutaneous lesions.

Small groups and single cases of ungual lesions of types not commonly seen in psoriasis have been reported from time to time.[7]

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4. Dubreuilh, W.: La pratique dermatologique, Paris, Masson & Cie, 1902, vol. 3.

5. Nägeli, O., in Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935, vol. 2.

6. Pardo-Castello, V.: Diseases of the Nails, Springfield, Ill., Charles C. Thomas, Publisher, 1936.

7. Aronstam, N. E.: A Preliminary Contribution to the Study of Onychopathies, Am. Med. **34**:393 (May) 1928; **35**:240 (April); 301 (May) 1929. Hoffmann, E.: Bemerkungen über das Psoriasisproblem und dabei beobachtete Nagelveränderungen (Kastendeckel- oder Doppelkantennägel), Med. Klin. **29**:737 (May 26) 1933. Louste, A., and Lévy-Franckel, A.: Psoriasis des ongles, Bull. Soc. franç. de dermat. et syph. **37**:100 (Jan.) 1930. Maschkilleisson, L. N.: Platonychia areata (psoriatica?) acuta, Dermat. Wchnschr. **88**:665 (May 11) 1929; A Rare Case of Disease of the Nails in Psoriasis, Urol. & Cutan. Rev. **34**:748 (Nov.) 1930. O'Donnell, J.: Two Interesting Nail Cases, M. J. Australia **2**:450 (Sept. 30) 1933. Pardo-Castello, V.: Diseases of the Nails, South. M. J. **27**:377 (May) 1934.

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PRESENT SERIES

The cases studied were taken from a series of cases of psoriasis recently studied from a statistical standpoint by Lane and Crawford.[8] In all cases there was typical psoriasis on other parts of the body, ungual changes considered to be psoriatic but unaccompanied with cutaneous lesions being excluded for the sake of accuracy. When the diagnosis of psoriasis of the nails was accepted in these cases, the possibility of fungous infections was kept in mind, and microscopic and cultural methods were used as a check in any cases in which doubt was possible. Syphilis was excluded by serologic tests when necessary. Other types of ungual change, such as dystrophy, eczema, and industrial injury, were differentiated by clinical appearance and by history.

In 49.8 per cent of 231 cases of psoriasis the finger nails were involved. This incidence is higher than that reported in any series in the literature. Finnerud [9] gave 25 per cent, which is the nearest of any to my figure. The greater incidence in my group might possibly be explained by the fact that this feature of psoriasis was being especially sought, or the discrepancy might be due to the relatively large number of cases of rather severe psoriasis in the group observed. Approximately one half (63 of 115) of the patients exhibiting lesions of the finger nails revealed changes in the toe nails as well. This was approximately one fourth (27.3 per cent) of the original 231 patients. In no case were lesions of the toe nails present without changes in the finger nails.

As shown in the tables, there was little variation in the types of changes in the finger nails and in the toe nails. When the toe nails were affected, the number involved more or less paralleled that of the finger nails.

Changes in color provided the most interesting feature, their incidence approaching that of pitting. Discoloration of the nail plate was found in almost two thirds of the cases, a surprisingly high number in view of the emphasis usually accorded such discoloration in textbooks. The incidence of discoloration in my series was only approximately 10 per cent lower than that of pitting. The discoloration starts with loss of luster, after which transparency decreases until complete opacity obtains, and the variation in color ranges from pure white through

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Rosenau, W. H.: Changes in the Finger Nails After Rheumatic Fever and Tuberculosis, J. A. M. A. **78**:1783 (June 10) 1922. White, C.: Onychia Due to Chronic Hypovitaminosis, ibid. **100**:2178 (June 30) 1934; Diseases of the Nails, Urol. & Cutan. Rev. **40**:562 (Aug.) 1936.

8. Lane, C. G., and Crawford, G. M.: Psoriasis: A Statistical Study of Two Hundred and Thirty-One Cases, Arch. Dermat. & Syph. **35**:1051 (June) 1937.

9. Finnerud, C. W.: Dermatologic Clinic: Psoriasis (Limited to the Nails and Scalp), M. Clin. North America **13**:445 (Sept.) 1929.

various shades of yellow to brown, sometimes a dark blackish brown. The colors described in textbooks include dirty white, yellowish white, dirty yellow, smoky yellow, yellowish brown, fawn, cloudy amber, dirty brown, grayish and blackish. In the present study the predominant hue was yellowish brown. This discoloration is most apt to begin near the distal margin of the plate, but may appear as an "island" anywhere. The lunula is rarely tinted unless the entire nail is affected and a generalized thickening takes place. The colored areas are mostly discrete and shade off fairly abruptly into the deep pink of the normal nail plate. Their size usually varies from 2 to 5 mm., but as much as half or two thirds of the plate may be discolored without thickening.

Changes in color may occur in the nails in a number of cutaneous diseases—notably eczema, onychomycosis, lichen planus, pityriasis rubra

TABLE 1.—*Distribution of Ungual Involvement in Two Hundred and Thirty-One Patients with Psoriasis*

	Fingers	Toes
Number of patients affected	115	63
Number of nails affected	836	441
Number of affected nails per patient (average)	7.3	7.0

TABLE 2.—*Types of Defects in Psoriatic Nails*

	Finger Nails		Toe Nails	
	Number	Percentage	Number	Percentage
Pitting	601	71.9	346	78.5
Discoloration	522	62.4	299	67.8
Thickening	30	3.6	19	4.3
Longitudinal ridging	16	1.9	9	2.0
Erosion	12	1.4	3	0.7

pilaris, dermatitis exfoliativa and ichthyosis—as well as in ungual dystrophies and numerous general systemic diseases. In such instances, however, the yellows and browns are not as conspicuous, and the whole plate is apt to be involved, without the sharp limitation usually seen in psoriasis. Syphilitic papules on the nail bed present a picture practically indistinguishable from that of psoriatic nails when general examination of the patient is not made. In view of the high incidence of discoloration of the nail plate in my cases of psoriasis, it was of interest to consult such works on dermatology as were available. There were twenty-eight of these in all,[10] and only thirteen, or less than half,

10. Andrews, G. C.: Diseases of the Skin, Philadelphia, W. B. Saunders Company, 1930. Arzt, L., and Zieler, K.: Die Haut- und Geschlechtskrankheiten, Berlin, Urban & Schwarzenberg, 1935. Besnier, E.; Brocq, L., and Jacquet, L.: La pratique dermatologique, Paris, Masson & Cie, 1900. Bloch, I.: Die Praxis der Hautkrankheiten: Unna's Lehren für Studierende und Aerzte zusammengefasst

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described changes in color with any degree of exactitude. Eight more mentioned changes in color without any qualification, and the remaining seven made no reference to color.

Pitting—stippling or punctiform depressions—is perhaps the most pathognomonic lesion of the nails in psoriasis. As indicated in table 2, pitting occurred in the present group of cases more frequently than any other change. The earliest manifestation of pitting is the appearance in the matrix of the nail of red points, practically always of a millimeter or less. The small cup-shaped depressions appear subsequently and always grow out with the plate, as they are fully formed before they reach the lunular margin. These pits, when seen beyond the lunula, usually appear as rather smoothly rounded depressions of fairly uniform size; they measure as a rule from 0.5 to 1 mm. in diameter, with a depth of about 0.5 mm. They may be distributed over the plate in any pattern and occur in varying numbers, from an isolated lesion up to such profusion as to make the nail resemble a thimble. While pitting is perhaps the least specific of all changes occurring in psoriatic nails, it often presents a somewhat distinctive appearance in this disease, the notable feature being that at first glance black dots rather than pits

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appear to be present. This is occasioned by the accumulation of cellular débris and extraneous material, which sticks rather tenaciously in the pits and makes the stippling more pronounced. The pitting is not always like this, however, and the occurrence of pitting in many other conditions militates against its being appreciably specific. Punctiform depressions have been frequently noted in onychomycosis, eczema, lichen planus, pityriasis rubra pilaris, exfoliative dermatitis, local trauma, local asphyxia and both acquired and congenital syphilis; during tuberculosis, rheumatic fever, chorea, severe anemia, Hodgkin's disease and bacterial endocarditis, and after Buerger's disease, cardiac block, empyema, scarlet fever and other acute febrile diseases. They also accompany some hereditary anomalies and dystrophies.

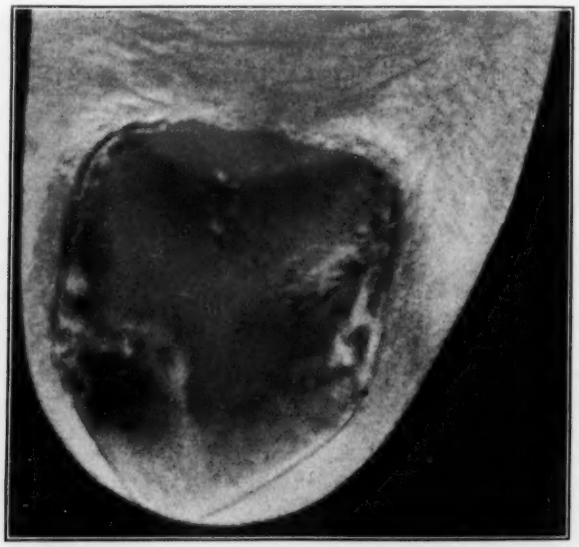

Fig. 1.—Psoriatic nail, showing changes in color, punctiform depressions and erosions.

Onychauxis, or thickening of the nail plate, was present slightly more often on the toes than on the fingers in my cases. This may be partially attributable to the pressure of shoes. The thickest nail found in this group was 5 mm. thick. These nails are the sites of the greatest variety of associated changes. They often become rigid and brittle and are always dry. The free edges frequently begin to crack and present a laminated appearance. These changes progress proximally, with softening, fragility and crumbling, and provide a worm-eaten surface. Onychomadesis, or complete loss of the nail plate, usually eventuates in such cases, and there is regrowth in due time. Onycholysis, a lifting up of the lateral edges of the nail plate, may occur independently of

onychauxis or in association with it. The free margins usually become elevated at the outer corners, and this process advances proximally, often completely overriding the nail folds, and as a rule leads to onychomadesis. The distal margin of the nail plate may turn down over the end of the finger in some instances; if this takes place in the presence of onychauxis it is called onychogryphosis. What may appear to be onychauxis alone is often found to consist of some thickening of the plate with marked hyperkeratosis of the nail bed, or the latter may be present without appreciable change in the plate itself. In the latter state large amounts of cellular detritus accumulates, and the plate becomes elevated throughout its extent. The large mass under the nail may become

Fig. 2.—Psoriatic nail, showing pitting and slight discoloration.

cornified and present a striking appearance; onychomadesis frequently follows. Onychauxis and all the changes described subsequent to it are found so often in ungual lesions of other cutaneous conditions that they are rendered entirely nonspecific.

Onychorrhexis, or longitudinal ridging, may occur in psoriatic nails but was not common in my series. The lesions usually extend throughout the length of the plate and vary in number from one or two to enough to make the surface appear corrugated. They are commonly not more than 0.5 mm. wide and high. Longitudinal grooves, of about the same caliber as the pits, may be found either accompanying the ridging or independently. These two types of changes are not peculiar to psoriasis.

Erosions of the nail plate were encountered less frequently than any other lesions but were of interest when present. They frequently occurred at the proximal end of the nail and at times involved the lunula. Their appearance was that of a sharp excavation, usually with perpendicular walls. They were of irregular shape and varied from areas 1 or 2 mm. in diameter up to those including nearly one third of the nail. The depth of the excavation was the entire thickness of the plate in some instances. Onychomadesis may but need not follow erosion. Minor excavations tend to accompany the softening and crumbling of onychauxis.

Any of the aforementioned types of lesion may occur in psoriasis of the nails as independent or isolated changes, and any combination

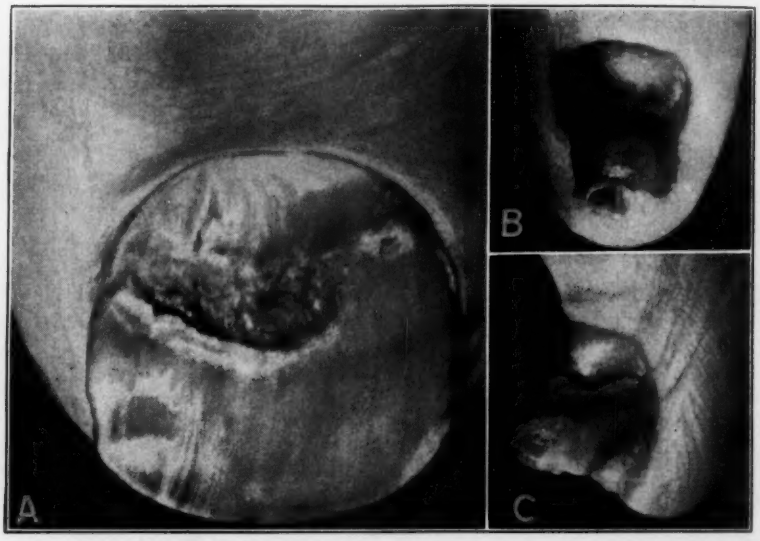

Fig. 3.—*A* shows a psoriatic nail with a large erosion and onychorrhexis. This did not lead to onychomadesis, as suggested by the appearance. The nail is intact on each side. *B* and *C* show two aspects of another nail, which illustrates severe onychauxis, downward lateral curvature of the plate, onychorrhexis and changes in the nail bed. There was subsequent onychomadesis.

of these malformations may take place. Other lesions that may be observed in psoriatic nails are not thought to be characteristic, as they may be found in any ungual condition of approximately the severity of psoriasis. Some of these are transverse grooves, platonychia, koilonychia, "box top nails" and onychatrophy.

Transverse grooves, known as Beau lines, are entirely nonspecific phenomena. They appear at the matrix as irregular transverse depressions of varying size and progress unchanged with the growth of the nail. They may occur singly or in succession, with corresponding ridges

between them. Beau lines may be found following any severe illness, especially when there has been prolonged fever, with any widespread cutaneous disease and subsequent to shock or local trauma. The physiologic transverse furrows of the newborn may be cited as a corollary.

Still other lesions that may be found in the nails in patients with psoriasis are those due to involvement of the matrix and the periungual tissue; with these this paper is not directly concerned. These include reddening extending from the nail fold under the plate to the bed, congestion of the matrix, lateral elevation of the plate, irregular growth, exaggerated convexity and encroachments by scaly and keratotic masses.

HISTOLOGIC FEATURES

I have been unable to secure a digit for histologic study of the ungual changes in psoriasis; hence in this phase of the subject I must employ the observations of others. A consensus shows the histologic picture to be analogous to that of psoriasis of the epidermis. The vessels of the subungual corium are greatly dilated, but there is little or no edema. There is an accumulation of leukocytes in the upper part of the corium and in the papillae. The epithelium of the hyponychium is acanthotic, with elongated rete pegs and extreme parakeratosis, and the usual microscopic leukocytic abscesses are present. In cases of severe disease the nail plate reverts to ordinary cornified integument, the cells of the basal layers returning to the epidermal type and forming eleidin instead of the onychogenic substance. Even the eleidin can disappear, and in the end the elemental histologic changes of psoriasis of the epidermis remain.

PATHOGENESIS

Pitting is due to local punctate injury to the germinal epithelium of the nail, which is of short duration and occurs preferably in the proximal portion of the matrix. It is doubtful whether such trauma could produce true pits if it took place as far out as the lunula. Dilated capillaries in the papillae provide these injuries and when located in the distal portion of the matrix may be seen as tiny red points, mentioned previously. Softening of the nail plate takes place over these capillary loops, and the devitalized cells fall out, leaving pits. Whether softening of previously normal horn cells takes place or cells with less than the usual amount of horn form is questionable. A focal punctate injury of long duration occurring in the germinal epithelium of the nail leads to the formation of grooving and ridging or onychorrhexis. These changes may thus be considered abnormalities in the process of cornification. True thickening of the nail plate itself results from disease of the entire matrix. Erosions, at least when situated at or close to the lunula, must likewise be due to lesions of the matrix of considerable

extent and severity. Changes in color which grow out from the matrix fall in the same category, the variations in color depending on abnormalities in the process of cornification and the resultant differences in the manner in which the light is reflected from them. All of these lesions may be considered as primary changes in the nail itself which when of sufficient gravity may go on to final loss of the plate.

All other malformations are secondary to hyperkeratosis of the nail bed; in many cases these may be the only changes observed. The accumulation of granular detritus in the nail bed may bring about change in the contour of the plate, elevation, thinning, brittleness, the entire range of discoloration, exfoliation of the surface cells and final loss of the nail. The formation of an isolated lesion somewhere in the center of the bed will not usually elevate the plate but may provide sufficient pressure to damage the horn cells and produce opacities and deviations in color. The imbibition of air by or between the abnormal plate cells may play some part in the reflected color.

DIFFERENTIAL DIAGNOSIS

In the differentiation of psoriasis of the nails from other ungual conditions, there are three diseases which must be considered first: eczema, exfoliative dermatitis and fungous infection. They not only resemble psoriasis in many instances but are the three commonest conditions, besides psoriasis, in which ungual changes appear.

Eczema of the nails always begins at the matrix and gradually progresses to the free edge. It may be manifested only by successive Beau lines following each recrudescence of the eczema on the skin. Changes in color are inconsistent in occurrence and type; dirty grays and blackish hues are frequently seen. Thickening of the plate or of the nail bed is variable but rather infrequent. Onychorrhexis is uncommon. Pits and erosions are more or less rare. Crumbling and splitting are apt to be found in cases in which the disease is severe, and onycholysis or onychomadesis may occur. Deformed nails are likely to replace those that fall. The picture is not infrequently complicated by paronychia. Ungual changes are not known to occur in eczema when the eruption of the skin is absent but may persist for several months after its disappearance.

Dermatitis exfoliativa is practically always accompanied with Beau lines, if nothing else. In cases of long-standing dermatitis onychauxis is usually observed, with more or less hyperkeratosis of the nail bed; onycholysis is common and onychomadesis frequent. Changes in color are almost the rule and vary from opacity to complete discoloration with any of the darker hues. Pitting may occur at times. Onychorrhexis and erosion are not at all common. Here again the nails may show evidence of the condition long after the skin has healed. Of course,

exfoliative dermatitis may supervene in psoriasis and show all the typical psoriatic changes in an exaggerated degree.

Fungous infection most commonly begins at the distal end of the nail plate and advances proximally. Dryness and loss of luster take place, with scaling and occasional focal discoloration. Changes in color vary widely, but an orange tint is frequently observed and may affect the entire nail more or less evenly. Some degree of onycholysis may occur. When the infection has reached the root, there is usually a succession of transverse grooves and ridges of the same type as the Beau lines. Destruction may be so extensive as to leave only a small dry crumbling stump centrally and proximally. When the nail folds are affected first, there may be only secondary changes in the plate, such as grooving and varying degrees of malformation, until the nail itself becomes invaded by the organism. Toe nails are at least as frequently involved as finger nails, and multiple involvement is the rule. Yeastlike organisms (Monilia, etc.) are almost always secondary invaders of the nail itself. Paronychia usually introduces the picture, with resultant small areas of adjacent nail destruction, and nearly any change in color may precede it in the area affected. The disease most commonly involves the fingers rather than the toes, and often only one or a few at a time. Mycotic nails may be seen without any cutaneous involvement. Neither thickening nor erosions are the rule; pitting and onychorrhexis are most uncommon.

There are numerous other ungual conditions which may at times closely simulate psoriasis, but usually there are insufficient changes to cause much confusion. In addition, the concomitant manifestations on the skin as a rule render identification relatively easy.

Dermatitis venenata, contact dermatitis and dermatitis industrialis, or trauma, may cause changes indistinguishable from those seen in eczema and hence may closely resemble psoriasis. Syphilis in its various stages may affect the nail plate, the nail bed or the periungual tissues and cause many manifestations similar to those of psoriasis. Pitting, thickening, ridging and discoloration are all seen, and less commonly destructive lesions are present. Occasionally subungual or periungual involvement brings about changes in the nails which strikingly suggest psoriasis and in the presence of a psoriasiform syphilid may lead to error in the best of clinics. On the other hand, there may be no concomitant syphilitic lesions, symptoms or history to clarify the picture, and the observation of pathologic changes in the nail becomes of paramount importance. In pityriasis rubra pilaris there may be striking ungual lesions consisting of gray or amber discoloration, striations, pitting, scaling, thickening, crumbling of the free edges and hyperkeratosis of the nail bed.

In lichen planus ungual changes, such as stippling, onychorrhexis, Beau lines, hyperkeratosis of the bed and papular paronychia producing

an appearance similar to that of eczema, are rare. In ichthyosis the nails are lusterless, longitudinally ridged, brittle and lamellated; there may be thickening, separation from the bed and various deformities of the plate. Hypovitaminosis (probably of vitamins B_2 and D) may result in dry, brittle, ridged and furrowed nails.

Occasionally ungual lesions that remotely resemble psoriasis are found in association with other conditions, such as pemphigus, pelade, various onychodystrophies including leukonychia striata and leukonychia totalis, poisoning with such metals as arsenic, mercury and silver and, in rare instances, eruption due to phenolphthalein.

SUMMARY

A study of psoriasis of the nails has been made and the more interesting and pertinent literature reviewed. Of 231 cases of psoriasis ungual lesions were present in approximately half. This incidence was double the highest previously recorded, and no infallible explanation can be offered. Finger nails were affected almost twice as often as toe nails. The principal changes observed, in order of frequency, were: pitting, change in color, onychauxis, onychorrhexis and erosion, the last three being relatively infrequent. Disturbances of the nail bed were observed fairly often. The most impressive feature of this study was the high incidence of changes in color of the nail plate, roughly two thirds of the 1,277 affected nails showing this phenomenon in some degree. This figure was only slightly below that for punctiform depressions. The predominant hue assumed by the nails was yellowish brown, although numerous colors have been mentioned by other authors. No special change in color is peculiar to psoriasis. Other features observed were nonspecific.

The pathologic picture and the pathogenesis of these lesions are discussed, so far as they are known. In the differential diagnosis of psoriasis of the nails three outstanding conditions are to be considered: eczema, dermatitis exfoliativa and fungous infection of the nail or of adjacent structures. In the final analysis these three cannot be separated beyond a reasonable doubt from psoriasis on the basis of ungual lesions alone. In certain cases the diagnosis will seem clearcut, but reliance will usually have to be placed on associated findings. The results of microscopic, serologic and other laboratory examinations are the determining factors in the absence of accompanying epidermal manifestations. This statement applies to a large number of other dermatoses and systemic diseases which occasionally show ungual changes resembling those of psoriasis. Treatment has been omitted from consideration, since it will be of little or no avail if directed to the nails alone and not to the disease as a whole.

SEROLOGIC PARADOX IN JUVENILE DEMENTIA PARALYTICA

REPORT OF A CASE

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INGLESIDE, NEB.

I shall report the results of serologic tests of the blood and of the spinal fluid in a case of juvenile dementia paralytica before, during and after the first phase of antisyphilitic treatment. A perusal of the literature fails to reveal any consideration of similar serologic findings. In view of the widespread interest in all matters pertaining to syphilis at this time and the consequent danger of too definite assumptions concerning the value and, above all, the meaning of serologic tests, I have decided to present this material. No attempt is made in this presentation to explain the phenomenon.

REPORT OF CASE

The patient, a white girl aged 11 years, is a foster child of farmers. Her intellectual and physical development were supposedly normal until the latter part of 1937, when her school grades gradually fell off, and she became more and more restless and slept poorly. On Thanksgiving, 1937, she experienced a sudden numbness of the left side of the face, the left arm and the left leg and had difficulty in talking. The attack lasted only a few minutes but was followed within the next few weeks by similar attacks. A local physician found the Wassermann reaction of the blood and of the spinal fluid to be "strongly positive" and the colloidal gold curve of the type found in dementia paralytica.

The patient was brought to the Hastings State Hospital for examination and consideration of treatment on Dec. 27, 1937. The physical, neurologic and other findings bore out the original diagnosis of juvenile dementia paralytica, and laboratory analysis showed a strongly positive Wassermann reaction of the blood and of the spinal fluid and a colloidal gold curve, determined both at the state and at the hospital laboratory, of the dementia paralytica type (5553322100 at Ingleside). The spinal fluid gave a strongly positive reaction for globulin and showed 72 cells per cubic millimeter. However, the Hinton test of the blood, done at Ingleside, gave a definitely negative result. (No flocculation test of spinal fluid is done at this laboratory, in view of the uncertain results thus far reported in this field, which are due, apparently, to the greater dilution of the substances concerned in the formation of floccules and precipitates.)

From Jan. 18, 1938, on, the patient was subjected to artificial fever therapy at weekly intervals, conjointly with intravenous administration of an arsenical preparation.

From the laboratory of Hastings State Hospital.

On January 21, a sample of blood was obtained, in order to check the Hinton reaction; this was again definitely negative, while both the Kline and the Wassermann reaction on the same sample were strongly positive.

After five fever treatments, on February 25, the blood was again tested. The Kline and the Wassermann reaction were strongly positive and the Hinton reaction definitely negative, regardless of the amount and proportion of serum used.

After the fever treatments had been completed (ten sessions), the spinal fluid was retested, on March 29, a few hours after the patient had received both fever and intravenous treatment. Blood was obtained on April 8. This time the result of the Wassermann test of the spinal fluid (performed on three dilutions) was reported as "doubtful" and the globulin content as slightly increased; there were only 6 cells per cubic millimeter, and the colloidal gold curve was of the "tabetic" type. The Wassermann, the Kline and the Hinton reactions of the blood were all strongly positive. When the Hinton test was repeated three days later on the same sample, the result was again definitely negative, whereas repetition of the Kline test at the same time and a week later with the same sample gave strongly positive results.

Chemical treatment was continued uninterruptedly, and on April 22 blood was again obtained; again the Wassermann, the Kline and the Hinton reaction were strongly positive. Repetition of the Kline and the Hinton test three days later with the same sample, however, gave, for the former, a persistently positive reaction and, for the latter, a reaction which, when the tube was centrifuged, barely permitted a reading of doubtful. The Kline reaction on the same sample persisted positive for two weeks, while the Hinton reaction became definitely negative. In all tests on the blood serum, the Kline and Wassermann reactions showed practically no variation in degree or type.

Clinically, the patient appears somewhat improved at present.

All Wassermann tests are done at the state laboratory in Lincoln, Neb., where a flocculation test on every specimen is also performed. The Kline test is performed at the Mary Lanning Memorial Hospital, at Hastings, Neb., with antigen obtained from LaMotte, Baltimore. For a little over a year I have performed the Hinton test (third modification) at the Hastings State Hospital as a routine on all patients. The results so far have been entirely satisfactory (except for some trouble with premature deterioration of the indicator in the early part of the summer of 1937), with a slightly greater sensitivity of the test, especially in treated patients, a result which was to be expected.[1] Prior to the experience reported here, I have encountered neither false positive nor false negative reactions. All samples from the patient reported on were run with several negative and one or two known positive specimens, and the latter were on all occasions run again, along with repeated tests of the same sample of this patient's blood. Both

1. Hollander, L.; Schlesinger, C. R., and Schmitt, C. L.: (*a*) The Hinton Test for Syphilis: A Study of Its Clinical Value in Three Thousand Patients, Urol. & Cutan. Rev. **39**:617 (Sept.) 1935; (*b*) The Hinton Test for Syphilis: The Second Study of Its Clinical Value in Three Thousand Patients, J. Lab. & Clin. Med. **22**:97 (Oct.) 1936; (*c*) The Hinton Test for Syphilis: The Third Study of Its Clinical Value in Three Thousand Patients, ibid. **23**:536 (Feb.) 1938.

old and fresh indicator were employed on the samples. All attempts to determine some exogenous factor which might have been held responsible for the observed reactions failed. As for the reagents employed, I have checked my own antigen with a sample prepared in Hinton's own laboratory and found no determinable difference. All other reagents are made up and all steps in the procedure taken strictly according to the originator's directions.[2]

Grund [3] refuted the assertion that a negative Hinton reaction of the blood serves to rule out involvement of the central nervous system, on the basis of his own experience. The results in the present case, prior to treatment, would bear out that author's thesis. As for the change of the reaction from negative to positive after treatment (*post hoc* or *propter hoc?*), independent not only of the behavior of the Wassermann reaction but of the closely related Kline flocculation reaction, and its subsequent rapid return to negative when the specimen was left standing, even Kahn's [4] exhaustive discussion of the factors involved in tests of this type fails to give an explanation that would permit anticipating such a reaction or eliminating the responsible factor.

It should be evident, and I stress the point, that the phenomenon herein reported does represent a false reaction and not an insufficiently sensitive test. The steps taken to control the findings are in accordance with the criteria laid down by Stokes,[5] who referred to the "reputation of being especially sensitive in latency" which the Hinton test is acquiring.

There is a tendency toward attaching too great importance to single determinations of the reaction of the blood with one type of test only, and the case reported will serve as another example of the value of performing more than one type of test as a routine, a point stressed by Hollander, Schlesinger and Schmitt,[1c] despite the fact that here a test giving a true reaction corroborated by other clinical and laboratory findings was fortunately obtained by the first test employed.

SUMMARY

A case of juvenile dementia paralytica is reported, in which a persistent false negative serologic reaction of the blood by one flocculation test occurred simultaneously with a strong true positive reaction by a

2. Hinton, W. A.: Syphilis and Its Treatment, New York, The Macmillan Company, 1936, pp. 294-300; personal communication to the author.

3. Grund, J. L.: The Exclusion of Neurosyphilis by Means of the Hinton Reaction of the Blood, Arch. Dermat. & Syph. **32**:569 (Oct.) 1935.

4. Kahn, R. L.: Serum Diagnosis of Syphilis by Precipitation, Baltimore, Williams & Wilkins Company, 1925.

5. Stokes, J. H.: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1936, pp. 115-148.

related flocculation test and by a Wassermann test. Subsequently, the false negative reaction became strongly positive and rapidly lost its positivity when the specimen was allowed to stand. The other serologic reactions remained constant or decreased in intensity during these variations.

The importance of performing more than one type of serologic test in the diagnosis of syphilis is stressed.

NOTE.—The Wassermann and the Hinton reaction of the blood were determined on blood obtained August 4. Both were strongly positive. There was an equally positive Hinton reaction five days later on the same sample. The patient is still receiving weekly injections of tryparsamide and thio-bismol.

TREATMENT OF HERPES SIMPLEX WITH MOCCASIN VENOM

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A preliminary report of the use of snake venom in the treatament of herpes simplex follows:

In March 1935, Peck [1] presented before the Section on Dermatology and Syphilis of the New York Academy of Medicine 3 cases of pemphigus treated with moccasin venom. He expressed the belief that he was dealing with a dermotropic virus and that the moccasin venom produced a barrier in the capillaries of the skin which the virus in the circulation could not break through to cause the clinical manifestations.

This report suggested that it might be worth while to investigate the possible influence of moccasin venom on herpes simplex. Moccasin venom with a dilution of 1:3,000 was given intradermally in 0.2 cc. doses. The local reaction was mild, and no constitutional symptoms were noted at any time. The patient was advised to make no local applications to the lesions at any time during treatment.

Fifteen patients with herpes simplex have been treated during the past three years. Since the disease is usually of short duration, an attempt was made to treat it only in the incipient stage, i. e., when itching, burning, swelling and slight vesiculation were present. A careful record was made in each case of the frequency of the attacks, the duration of the subjective symptoms, the length of time between the appearance and the disappearance of the stage of vesiculation and the duration of the whole attack, from the appearance of the first symptoms to the end of the crusting stage. The following facts were noted: In 12 cases in which treatment was begun early, i. e., within from eight to twenty-four hours after onset (when the patient noted burning and itching followed by swelling and beginning vesiculation), the subjective symptoms disappeared within from five to twelve hours after injection of snake venom and the swelling and vesiculation within from twelve to thirty-six hours, the vesicles being replaced by small dry crusts with no exudation. However, in 3 other cases, in which the eruption had been present for longer than twenty-four hours, the duration and course of the disease were unaltered, although

1. Peck, S. M.: Pemphigus Treated with Moccasin Venom, Arch. Dermat. & Syph. **33**:150-151 (Jan.) 1936.

the patients stated that the subjective symptoms were noticeably lessened.

The cases to be reported illustrate the course of the disease under this treatment:

REPORT OF CASES

CASE 1.—In July 1935 R. K., a man aged 33, complained of recurrent herpes simplex of the lower lip, three attacks having occurred during the previous nine months. Various local applications had been used, without appreciable relief. The duration of the disease, from the appearance of the initial symptoms of burning and itching through the stage of vesiculation and exudation was approximately five or six days. When he was first seen by me, the eruption had been present for twelve hours. There were itching and burning and a sense of fulness on the left side of the lower lip. Beginning vesiculation was apparent. The patient was given 0.2 cc. of moccasin venom with a dilution of 1:3,000 in the left forearm. When seen approximately twenty-four hours after the injection, he stated that the burning, the itching and sense of fulness had disappeared in approximately six hours. Examination of the affected area showed that the swelling had disappeared, and in the place of the vesicles there were small dry crusts. The patient was seen three times in the next seventy-two hours, during which time there was no recurrence of either the subjective or the objective symptoms.

Questioned concerning the usual course of the disease, the patient stated that within from twenty-four to forty-eight hours the stage of vesiculation was followed by exudation, which remained one or two days and was followed by heavy crusting.

This patient was seen two and one-half years ago; when recently interviewed, he had had no recurrence.

CASE 2.—L. H., a woman aged 31, was seen in July 1935, when she complained of a "cold sore" on the left side of the lower lip of about eighteen hours' duration. She stated that there were sensations of swelling and burning. Objectively, there were some slight erythema and three or four small vesicles, as well as beginning intumescence. There had been some six or eight similar attacks during the last year. The duration of these attacks, from the initial symptoms through the stages of vesiculation, exudation and crusting, was approximately fourteen or fifteen days.

The patient was given 0.2 cc. of moccasin venom intradermally and advised to apply nothing locally to the lesion. At the end of four days there was no evidence of the eruption.

The patient was again seen on April 5, 1938, at which time she had beginning herpes simplex of the right side of the upper lip of about eight hours' duration. Swelling burning and a sense of fulness were accompanied with beginning vesiculation. She was given 0.2 cc. of moccasin venom intradermally. When she was seen again on April 6, the swelling and burning had gone, and the vesiculation was replaced by small dry crusts. However, on April 8, the patient returned with a new lesion at the posterior aspect of the orifice of the left nostril. This lesion was the size of a pea, erythematous and tender; burning was present, and there were five pinhead-sized vesicles. She was again given 0.2 cc. of snake venom with a dilution of 1:3,000 intradermally. She was next seen on April 12, when she stated once more that the burning and the itching had disappeared within twenty-four hours. Objectively, the lesion had shrunk, and the vesicles were replaced by small dry crusts.

For many years before July 1934 this patient had been subject to recurrent attacks of herpes simplex on the lips and about the nose during the summer months. After the injection of snake venom in 1934 she had one recurrence in the summer of 1936, which disappeared in forty-eight hours, there being only slight vesiculation and swelling. No treatment was received for this attack. The next recurrence was that described as of April 1938.

CASE 3.—M. L., a woman aged 30, was first seen on Jan. 6, 1938, at which time she complained of swelling, burning and itching of the left ala nasi of two days' duration. There were some vesiculation and much crusting. She was given 0.2 cc. of moccasin venom with a dilution of 1 : 3,000 intradermally.

When she was seen again on January 7, there was no apparent change, although she stated that the swelling seemed less and there were no further burning and itching. She was given a second similar dose of moccasin venom on this date. The patient was next heard from by telephone on January 9, at which time she stated that the lesion had practically disappeared.

In this case the lesions had appeared three or four times yearly for ten years. The usual course of the disease, according to the patient, was ten or twelve days.

The patient was seen again on April 15, with herpes simplex at the orifice of the left nostril. The lesion was the size of a pea and accompanied with burning and itching and four small vesicles. It had been present for approximately sixteen hours. Moccasin venom (0.2 cc. of 1 : 3,000 dilution) was given intradermally. Twenty-four hours later the subjective symptoms had entirely gone; the swelling had receded, and the vesicles were replaced by small dry crusts.

This case illustrates the difference in the response to moccasin venom when it is given in the early stages of herpes simplex and when it is given at the height of the eruption.

CASE 4.—M. A., a woman aged 23, a nurse, on March 5, 1937, complained of recurrent herpes simplex lateral to the left commissure of the mouth. The patient stated that during the past eight months she had had seven such lesions. The duration of the disease was usually twelve or fourteen days. The current eruption was of thirty hours' duration and consisted of an erythematous patch 2 cm. in diameter, which was accompanied with itching, burning, slight swelling and slight vesiculation. Moccasin venom (0.2 cc. of 1 : 3,000 dilution) was given intradermally.

The patient was seen twenty-four hours later, at which time the subjective symptoms had disappeared and the vesicles were replaced by small crusts. Forty-eight hours later the swelling had receded, and there were only slight residual erythema and crusting. There was no exudate.

COMMENT

From October 1936 to January 1937 an attempt was made to determine what, if any, effect moccasin venom would have on the virus of herpes simplex. Dr. Samuel B. Frank, of the Vanderbilt Clinic, Columbia University, who had isolated a strain of this virus, made three experiments with rabbits:

1. The rabbits were inoculated with equal parts of the virus and of moccasin venom with a 1 : 3,000 dilution.

2. The rabbits were inoculated intradermally with 0.2 cc. of moccasin venom and the virus given them subsequently.

3. The virus was given, and when vesiculation appeared, 0.2 cc. of moccasin venom was given intradermally.

In none of these experiments was the course of the eruption influenced.

In 3 cases herpes zoster was treated with intradermal injections of moccasin venom. In my opinion, the course of the disease appeared to be unaltered. However, the patients, each of whom had complained of severe burning and itching when first seen during the stage of vesiculation, stated that the subjective symptoms were alleviated.

SUMMARY

Fifteen patients with herpes simplex and 3 with herpes zoster were treated between July 1934 and the present time with moccasin venom in 1 : 3,000 dilution.

From personal observation and the statements of the patients, I feel that the course of this eruption was materially shortened by this form of therapy.

Attempts to influence the virus directly by the use of moccasin venom with 1 : 3,000 dilution in experiments on rabbits were unsuccessful.

While no claim can be made on immunization against herpes simplex by the use of moccasin venom, nevertheless, in many cases in which there had been repeated recurrences, the number of such recurrences seemed to have been materially decreased.

140 East Fifty-Fourth Street.

MULTINUCLEATED (GIANT) CELL TUMOR OF THE GUM (EPULIS)

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Dermatologists are frequently called on to consider morbid processes of the oral cavity. Tumors of the gum offer special difficulties. Histologic study reveals the many possibilities which must be taken into consideration when a tumor is seen.

The confused state of the information on this subject furnishes the main reason for this investigation. We found classification as to age, location and type extremely variable, the confusion of the classification according to type being present only because there is as yet no one standard of pathologic nomenclature for the interpretation of these neoplasms. The reports of individual cases have not been extensive enough to justify drawing definite conclusions.

DEFINITION

Epulis, according to Dorland,[1] is derived from the Greek ἐπί (on) and οὖλον (gum). It was first used by Virchow in a topographic sense, denoting any tumor on the gum. The term "tumor" is a clinical one and refers to any lesion larger than a nodule. Such lesions may result from an inflammatory (simple or granulomatous) or neoplastic process. Thus it is readily understood why diagnoses of inflammatory epulis, granulomatous epulis and neoplastic epulis are reported.

Congenital tumors of the gum are rare and have been reported under the term congenital epulis. Das [2] described the case of a Hindu baby, who had a large growth on the gum at birth. Pathologically the mass was a fibroma. Kaempfer [3] reviewed 8 recorded cases. In 4 of these epithelial inclusion cysts were found. He added a case of his own and suggested the term "odontoblastoma." In a review covering sixty years, Kuhne [4] found a total of 15 cases on record.

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1. Dorland, W. A. N.: American Illustrated Medical Dictionary, ed. 15, Philadelphia, W. B. Saunders Company, 1929.
2. Das, P. S.: Lancet **2**:182, 1933.
3. Kaempfer, L. G.: Surg., Gynec. & Obst. **12**:357, 1911.
4. Kuhne, W.: Beitr. z. Anat., Physiol., Path. u. Therap. d. Ohres **31**:94, 1933.

Tumors of the gum developing during pregnancy have been reported as "pregnancy epulis" by Tratman [5] and Blum.[6] Microscopically they have been found to be fibroma, "angiogranuloma" of Rywkind,[7] giant cell granuloma and hypertrophy of the gum. Blum reported 16 of his own cases, in 10 of which he especially classified the growth as pregnancy tumor. He cited Arkövy [8] as support for the contention of a possible endocrine etiologic factor. He was supported in this regard by Monash.[9]

Tumors frequently form on the gum as a result of an inflammatory process, especially when of long duration. These are included under the term inflammatory epulis. Such a process is usually due to sequelae of poor dental hygiene, such as infections, dental caries, broken-off roots, jagged teeth and calculus formation. Clinically there result hypertrophic gingivitis, granulation tissue and scar formation. These conditions may be diffuse or local.

Granulation tissue and scar formation have been classified by some as granulomatous epulis [10] with no regional pathologic changes.

Neoplastic epulis will be described more fully later.

Many authors have borrowed the clinical term epulis for a pathologic diagnosis. Clinically, the term is a poor one and is no more diagnostic that the term "dermatitis." The tumor most commonly referred to as an epulis is a multinucleated or giant cell tumor. The former appelation is an improvement over the latter, as the one describes the type and the other merely the character of the cells.

Giant cell tumors are found in various locations. They appear singly in the soft tissues of the gums, on the palate, in the joints and along the tendon sheaths of the hands and feet. The marrow cavities at the epiphysial ends of long bones and the jaws are the sites of the localized bony lesions. The generalized form of giant cell tumor of bone occurs in association with osteitis fibrosa of hyperparathyroidism (Hunter and Aub [11]; Jaffe, Bodansky and Blair [12]).

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5. Tratman, E. K.: J. Am. Dent. A. **21**:2201, 1934.

6. Blum, T.: J. Am. Dent. A. **18**:393, 1931.

7. Rywkind, A. W.: Virchows Arch. f. path. Anat. **263**:415, 1927.

8. Arkövy, cited by Blum,[6] p. 406.

9. Monash, S.: Proliferative Gingivitis of Pregnancy: Report of Cases, Arch. Dermat. & Syph. **24**:580 (Oct.) 1931; Surg., Gynec. & Obst. **42**:794, 1926.

10. Thoma, K. H.: Clinical Pathology of the Jaws, Springfield, Ill., Charles C. Thomas, Publisher, 1934.

11. Hunter, D., and Aub, J. C.; Quart. J. Med. **20**:123, 1927.

12. Jaffe, H. L.; Bodansky, A., and Blair, J. E.: Proc. Soc. Exper. Biol. & Med. **27**:710, 1930; Fibrous Osteodystrophy (Osteitis Fibrosa) in Experimental Hyperparathyroidism of Guinea-Pigs, Arch. Path. **11**:207 (Feb.) 1931.

HISTORICAL REVIEW

Lebert [13] and Paget [14] were the first to describe giant cell tumors. As a result of his study of 46 cases Nélaton [15] was the first to regard them as benign. A profusion of names have been applied to this lesion in the literature, including giant cell sarcoma, giant cell epulis,[16] giant cell tumor,[17] benign giant cell sarcoma,[18] myeloid sarcoma or osteoclastoma [19] and tumeur à myeloplàxes.[15] Not until the underlying causative factors are more fully understood will it be possible to simplify this confusing nomenclature.

DIAGNOSIS

Multinucleated (giant) cell tumors are the commonest of those found on the gums. They arise most frequently anteriorly, between the teeth from the periosteum of the alveolar margin, but at times are found farther back, even between the molars. Their origin from a tooth socket is not uncommon. They are usually from 1 to 2 cm. in diameter but may be two or three times this size. They vary from dull red to dark bluish red and are covered with mucous membrane. They are usually smooth, at times lobulated and semifirm. They do not readily ulcerate or bleed and usually are not painful.

Pathologically the mass may be seen to extend throughout the deep, the middle and the upper portion of the cutis; it is well circumscribed but not encapsulated, in the sense that there is a definite fibrotic process around it. The mucous membrane as a rule is thin, flattened and bandlike, and the rete pegs and papillary bodies obliterated. If the mass has been present for a considerable time, the epidermis may show marked irregular acanthosis.

The tumor is composed of a fibrous stroma, which as a rule is not prominent. There is a dense cellular infiltrate. Within the fibrous stroma there may be a moderate number of somewhat dilated blood vessels. About the mass the vessels are more dilated and occasionally filled with blood elements. The cellular elements of the tumor are small round cells, multinucleated cells and a larger number of variously sized

13. Lebert, M.: Physiologie pathologique, Paris, J. B. Baillière, 1845, vol. 2, p. 121.

14. Paget, J.: Lectures on Surgical Pathology, Philadelphia, Lindsay & Blakiston, 1871, lecture 27, pt. 2, pp. 544-557.

15. Nélaton, E.: Tuméurs benignes des os ou tumeurs à myeloplàxes, Paris, A. Delahaye, 1860.

16. Bunting, R. W.: Oral Pathology, Philadelphia, Lea & Febiger, 1929.

17. Stout, A. P.: Human Cancer, Philadelphia, Lea & Febiger, 1932.

18. Hayes, L. V.: Clinical Diagnosis of Diseases of the Mouth, Brooklyn, Dental Items of Interest Publishing Co., Inc., 1935.

19. Ewing, J.: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928, p. 259.

spindle cells, the smaller ones predominating. The multinucleated (giant) cells present a striking feature: Many of these cells contain a varying number of nuclei (from a few to a hundred), which may be arranged at the periphery, in the center or on one side. Moreover, more than one type of grouping may be seen in the cells in the same section. It is difficult to make any definite deductions from the various types of multinucleated (giant) cells alone. Their cytoplasm, as a rule, is more or less homogeneous, opaque and acidophilic. There are no mitotic figures as in malignant processes. Neither involvement of the regional lymph nodes nor metastases have been noted. The periosteal cells show no evidence of proliferation. There is no invasion of the periosteum by giant cells.

The pathologic picture just described is identical with that of the localized form of giant cell tumor occurring eleswhere, as well as with the generalized tumors of osteitis fibrosa. In the latter condition fibrosis is a marked feature in the late stages; hence the name.

Leukemia	(*a*) Myelogenous (*b*) Lymphatic
Angioma	(*a*) Hemangioma (*b*) Lymphangioma
Granuloma	(*a*) Granuloma pyogenicum (1) Granuloma fissuratum (*b*) Granulation tissue (*c*) Syphilis (1) Chancre (2) Gumma (*d*) Tuberculosis
Fibroma	(*a*) Soft (1) Papilloma (*b*) Hard (2) Neurofibroma
Sarcoma	(*a*) Round cell (1) Small cell (2) Large cell (*b*) Spindle cell (1) Small cell (2) Large cell (*c*) Lymphosarcoma (*d*) Kaposi sarcoma (*e*) Fibrosarcoma
Carcinoma	(*a*) Prickle cell epithelioma (*b*) Basal cell epithelioma (*c*) Nevocarcinoma (*d*) Bowen's disease (*e*) Metastatic tumor

Differential Diagnosis.—The disease must be differentiated.

The differential clinical features are few. As we shall show later, there are many reasons for the lack of clinical variation.

Leukemia: The occurrence of hard nodular swellings on the gums in lymphatic [20] and in myelogenous [21] leukemia has been reported. Irregular hypertrophy with extension of the gingiva over the teeth toward the occlusal surface is seen. Petechiae often occur in the mucous membrane and the skin. Examination of the blood and puncture of the bone marrow establish the diagnosis. It should be noted

20. Goadby, K.: Diseases of the Gums and Oral Mucous Membrane, ed 4, New York, Oxford University Press, 1931, p. 374.

21. Mead, S. V.: Diseases of the Mouth, ed 4, St. Louis, C. V. Mosby Company, 1932, p. 350.

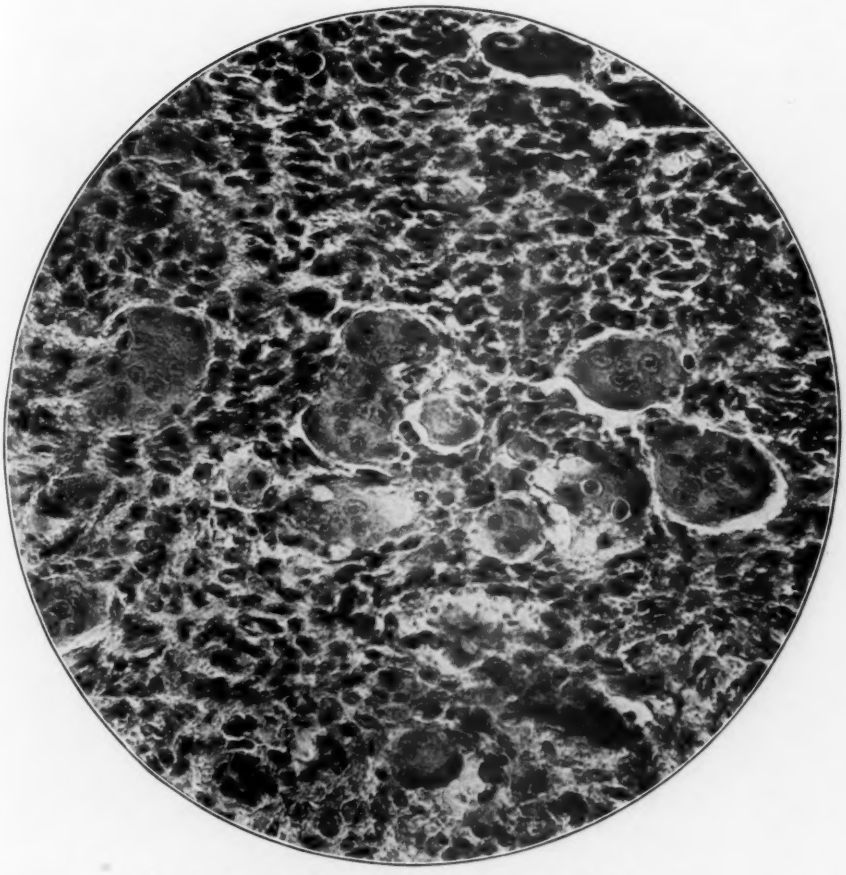

Fig. 1.—Multinucleated (giant) cell tumor of the gum.

Fig. 2.—Multinucleated (giant) cell tumor of eight months' duration in a woman aged 39.

that acute stomatitis may be associated with leukemia. The finding of Vincent's organisms should not lead one to overlook this more important possibility.

Angioma: Angioma is composed of dilated vessels, at times of various sizes with few or no cellular elements. There are types which are composed of larger vessels, the walls of which are part of the framework of the cutis so that the endothelial lining is distinct but there is no sharp margin between the wall of the vessel and the cutis. When the blood vessels are involved, the condition is known as hemangioma. At times large irregular sinuses extend into the deep tissue as in cavernous angioma. When the lymph vessels predominate, the condition is lymphangioma.

Tuberculosis: Tuberculosis of the gums is relatively infrequent and is usually secondary to pulmonary tuberculosis. The lesion is ulcerated and covered with a gray or grayish yellow secretion. The margin is irregular and may or may not be undermined. The border is indurated, and the lesion is painful. The histologic picture of tuberculosis requires no elaboration.

Syphilis: Chancre of the gum is rather infrequent. Klauder [22] gave an extensive review of extragenital chancre with special consideration of chancre of the gum. Epstein and Ziegler [23] reported a case more recently. It may be difficult to differentiate the condition from gumma on the clinical picture alone. The chancre starts superficially and the gumma deeply. The chancre is a sharply marginated, indurated, eroded papule or nodule. The regional lymph nodes are enlarged, hard and shotty. The gumma is usually larger, more deeply seated and ulcerated.

Pathologically the condition is true granuloma, made up of granulation tissue; the outlying vessels are thickened, with intimal proliferation and a perivascular plasma cell infiltrate. About the gumma may be some fibrosis, and the center may be necrotic.

Granuloma pyogenicum: Granuloma pyogenicum (telangiectaticum) is composed predominantly of numerous greatly dilated thin-walled small vessels, irregular in size and shape, many of which are filled with blood elements. The stroma may be loose and lacy or contain many cells simulating the endothelial type.

Granuloma fissuratum, as described by Sutton Sr.[24] and Sutton Jr.[25], is granuloma pyogenicum folded on itself and growing in the mucobuccal fold.

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22. Klauder, J. V.: Chancre of the Gum, with Report of a Case, Arch. Dermat. & Syph. **3**:615 (May) 1921.

23. Epstein, C. M., and Ziegler, E. P.: J. Am. Dent. A. **2**:2228, 1933.

24. Sutton, R. L., Sr.: Granuloma Fissuratum, Arch. Dermat. & Syph. **26**: 865 (Nov.) 1932.

25. Sutton, R. L., Jr.: A Fissured Granulomatous Lesion of the Upper Labio-Alveolar Fold, Arch. Dermat. & Syph. **26**:425 (Sept.) 1932.

Granulation tissue tumors are frequent. They appear in various stages, often with organization.

Fibroma: In soft fibroma the vessels are somewhat dilated and the connective tissue stroma is loose and somewhat edematous. The hard fibroma includes neurofibroma, which may be single or multiple (Recklinghausen). Hard fibroma is made up of dense fibrous bands extending in different directions and containing a cellular infiltrate. As a rule, this infiltrate is rather sparse and is composed of fixed connective tissue cells. Occasionally the cellular infiltrate is rather prominent but orderly, as in neurofibroma or cellular fibroma.

At times the infiltrate may contain a considerable number of fibroblasts (fibroblastoma). Papilloma may be included under soft fibroma.

Sarcoma: The division of sarcoma into spindle cell, round cell and giant cell types does not classify the subject sufficiently, according to Ewing.[19] Aside from the so-called giant cell type, sarcoma is rarely found on the gingiva. In general, there is a dense cellular growth in different arrangements and extending in many directions. The outline of the mass is ill defined, and individual cells or strands of cells extend between the collagen bundles. The connective tissue framework is usually scant within the tumor. When it is present in an appreciable amount, the neoplasm is called fibrosarcoma. The particular subdivision of sarcoma depends on the tissue from which the tumor arises, as well as the type and size of cell.

Fig. 3.—*A*, Organizing granulation tissue of one year's duration in a woman aged 33; *B*, lymphosarcoma with its primary site on the gum in a man aged 37. The tumor was of eight months' duration at the time this photograph was taken. The patient died one year later.

Multiple idiopathic hemorrhagic sarcoma, or Kaposi sarcoma, is unusual in the mouth.[26] We have found no references to lesions on

26. Feldman, S.: Sarcoma Kaposi (?), Arch. Dermat. & Syph. **27**:692 (April) 1933. Gross, P.: Multiple Idiopathic Hemorrhagic Sarcoma (Kaposi) with Lesions in the Mouth, ibid. **30**:153 (July) 1934.

the gum. The subject has been completely reviewed recently by MacKee and Cipollaro.[27] In lymphosarcoma the infiltrate is composed of lymphoid tissue. The clinical picture and the lack of changes in the blood are necessary for accurate diagnosis.

Carcinoma: Carcinoma of the gums begins as an ulcer or papillary tumor. In a late lesion the visible portion may be insignificant, while the deeper portion infiltrates the jaw or extends to the floor of the mouth.

Carcinoma of the gum [28] is most often of the prickle cell type. The epidermis is irregularly acanthotic and about it are usually a productive type of protective reaction, plasma cells and fibrous connective tissue (desmoplasia). On the gums it is uncommon to find a reaction composed only of small round cells. The prickle cells are of various sizes and shapes, the staining characteristics are altered and the cells have lost their relation to one another (anaplasia); whorls and pearls, keratinization and mitotic figures may or may not be present. The neoplasm may be intraepidermal or extraepidermal, en masse, infiltrating or disseminated.

Basal cell epithelioma of the mouth is rare only a few cases having been recorded. In none of these was the lesion on the gums. The pathologic picture is the same as that in lesions on the skin. Krompecher,[29] Siegmund and Weber [30] and Spring [31] all pointed out the close resemblance of the histologic picture of adamantinoma to basal cell epithelioma of the mucous membranes.

Cases [32] of oral and gingival primary and metastatic nevocarcinoma containing pigment have been recorded. A case of primary nevocarcinoma of the gum without pigment will be reported later by one of us. Biopsies of primary and of metastatic lesions corroborated the diagnosis. Pathologically nevocarcinoma is composed of large, somewhat rounded or polyhedral cells with definite cell bodies and fairly large, lightly stained round vesicular nuclei. The cells may be of similar or varying sizes and penetrate through the cutis into deeper structures, depending on the duration and the degree of malignancy. Nests of similar cells are found in the lower margin of the epidermis.

Bowen's disease of the mouth is probably rare. No reports were found describing the condition on the gums. The pathologic changes

27. MacKee, G. M., and Cipollaro, A. C.: Am. J. Cancer **26**:1, 1936.

28. Satenstein, D. L.: Histologic Evidence of Epithelioma of the Skin, Arch. Dermat. & Syph. **33**:48 (Jan.) 1936.

29. Krompecher, E.: Beitr. z. path. Anat. u. z. allg. Path. **28**:1, 1900; **64**:165, 1919.

30. Siegmund, H., and Weber, R.: Pathologische Histologie der Mundhohle, Leipzig, S. Hirzel, 1926.

31. Spring, K.: Ztschr. f. Stomatol. **30**:455 and 608, 1932.

32. Norrie, F. H. B.: J. Laryng. & Otol. **49**:49, 1934.

are those of malignant dyskeratosis; the cells are large, round and of varying size. The cytoplasm appears washed out. The nuclei are of different sizes, some being very large. Many of the cells are multinucleated. These cells may be found as high as the upper border of the epidermis.

Metastases from many primary internal malignant growths occasionally find their way to the gingiva. The metastasis may duplicate the primary growth or be more or less differentiated.

CORROBORATIVE DIAGNOSTIC EVIDENCE

On clinical findings alone it is often impossible to differentiate various gingival tumors. The vascularity, the bony base, the structure of the tissue overlying this base and the continual moist environment are some of the causes of the lack of clinical variation. The study of a tumor of the gum must include clinical data as well as laboratory findings. The duration, development and rate of growth are first determined. Then the history—the wearing of irritating dentures, the occurrence of bleeding and ulceration and the presence of pain—should be investigated. Manifestations of generalized dermatologic lesions are often seen in the mouth. Metastases may find their way to the jaws from many internal malignant growths.

Laboratory examinations are indispensable. Roentgen examinations readily differentiate central from peripheral tumors. Positive roentgen findings in cases of gingival tumors speak more for carcinoma or sarcoma of the gum. These neoplasms more than others tend to invade bone. Special examinations of the blood and bacteriologic and mycologic investigations are indicated in cases of suspected leukemia, syphilis, tuberculosis and pyogenic and fungous processes. Dark field examination and the Klein test may be the only methods of determining the presence of early chancre.[33]

In neoplastic processes of the gum clinical diagnosis cannot always be absolute and at best can only be suggested. For positive diagnosis examination of tissue is necessary. This does not mean that small pieces should be taken from every tumor of the gum or of the mouth. When the clinical diagnosis is suggestive of a benign process the entire mass may be removed by methods accepted for that particular condition. The specimen may then be sent to a laboratory for pathologic corroboration. Should the pathologist's opinion corroborate that of the clinician, all is well and good; if not, further procedures should be instituted at once as the case warrants. If the mass is suggestive

33. Chargin, L.; Eller, J. J., and Rein, C. R.: The Microscopic Slide Precipitation Test for the Diagnosis of Syphilis with Chancre Fluid, Arch. Dermat. & Syph. **26**:965 (Dec.) 1932.

of a malignant process, a fair-sized piece should be removed for study, and on the pathologic interpretation the treatment and prognosis will depend. Bloodgood [34] and MacKee and Satenstein [35] averred that there is almost no possibilty of disseminating tumor emboli to distant parts by careful removal of material for biopsy. Ewing,[19] Bland-Sutton [36] and Boyd [37] expressed agreement with this view.

MALIGNANCY

There is no evidence that giant cell tumors ever metastasize. It is rare that these tumors erode the neighborhing bone without undue trauma or some other causative factor. However, if incompletely excised, the tumor is prone to recur locally without histologic change. None of the microscopic features suggest malignancy. Only a single indubitable giant cell tumor has been described as becoming malignant (Ewing). This developed only after repeated insults by surgical measures and irradiation.

TREATMENT

Local anesthesia with excision of the tumor and curettage is usually sufficient, if followed by electrocoagulation or the application of an escharotic. When more radical treatment is necessary the associated periosteum may be resected. At times one or two involved teeth must be extracted. A mutilating operation is inexcusable. It is inadvisible to employ radium.[38] Cure is usually obtained, but there may be serious sequelae.[39]

PATHOGENESIS

Is the multinucleated (giant) cell tumor of neoplastic or inflammatory origin? The literature on the subject is voluminous and largely inconclusive. However, we have almost invariably found this tumor classified as benign sarcoma.

Von Albertini [40] identified it as true blastoma and asserted that the spindle cells are true mesenchymal tumor cells and that the tissue

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34. Bloodgood, J. C., in Lewis, D.: Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1930, vol. 4, chap. 14, p. 161. Greenough, R. B.; Simmons, C. C., and Harmer, T. W.: J. Orthop. Surg. **3**:602, 1921.

35. MacKee, G. M., and Satenstein, D. L.: Personal communication to the authors.

36. Bland-Sutton, J.: Tumours, Innocent and Malignant: Their Clinical Characters and Appropriate Treatment, ed. 7, London, Cassell & Co., 1922.

37. Boyd, W.: Surgical Pathology, Philadelphpia, W. B. Saunders Company, 1925.

38. Fischel, E.: S. Clin. North America **5**:1263, 1925.

39. Soiland, A., and Castlow, W. E.: Am. J. Roentgenol. **23**:639, 1930.

40. von Albertini, A.: Gutartige Riesenzellgeschwülste, Leipzig, Georg Thieme, 1928.

is of immature and embryonic type. Ritter [41] expressed the belief that the cells of the vessel walls are the source of both the spindle and the giant cells. He thus identified the process as one primarily involving the reticuloendotheial system.

Giant cell tumors were induced experimentally by Miner [42] and Rhode.[43] The former author used sterilized "tartar" from teeth, and the latter, powdered calcium carbonate. The soft tissues into which the material was injected were incited to a foreign body type of response. Sections of the induced lesions showed a picture closely resembling that of multinucleated (giant) cell tumor containing particles of the calcium salt. Delater and Bercher [44] have expressed the opinion that epulis and even granuloma of the jaw are always initiated by a growth of paradental epithelial débris.

Taking into account the singular action of the periosteum of the alveolar border in the shedding of deciduous teeth, Geschickter and Copeland [45] have correlated normal osteoclastic hyperplasia with the age incidence and location of multinucleated (giant) cell tumor. They stated that this condition does not occur before the age of 5 years. The shedding of deciduous teeth occurs from the sixth to the thirteenth year. They go further to say that epulis practically never occurs at the site of the molar teeth and never at that of the third molar. Unlike all other teeth, the molars make but one appearance.

The discovery of hyperparathyroidism in osteitis fibrosa with giant cell tumors seems to add further support to the theory of resorption and repair. Further consideration of multinucleated (giant) cell tumor from the endocrinologic point of view might be valuable.

That the tumor arises from the alveolar margin of the periosteum is almost unquestionable. Yet the role of the periosteum in its formation is still indefinite. The presence of small islands of bone frequently seen is as yet unaccounted for.

SUMMARY AND CONCLUSIONS

The inexactness of the general term "epulis," which fails to reveal the true nature of a gingival tumor, is pointed out.

The term "multinucleated (giant) cell tumor" is suggested for the lesions so common in this region. This describes the type and size of the more striking of the cellular elements. The word tumor is correct whether the process is inflammatory or neoplastic.

41. Ritter, K.: Deutsche Ztschr. f. Chir. **54**:1, 1900.
42. Miner, L. M. S.: J. Allied Dent. Soc. **7**:429, 1921.
43. Rhode, C.: Surg., Gynec. & Obst. **41**:740, 1925.
44. Delater, J., and Bercher, J.: Bull. et mém. Soc. anat. de Paris **94**:191, 1924.
45. Geschickter, C. F., and Copeland, M. M.: Recurrent and So-Called Metastatic Giant Cell Tumor, Arch. Surg. **20**:713 (May) 1930.

The benign nature of multinucleated (giant) cell tumor of the gum has been described. The condition is prone to recur locally, however, if the treatment is incomplete.

The treatment of choice is excision, with curettage and coagulation, the involved teeth and periosteum being sometimes included. The dangers of irradiation have been noted.

The use of the word "sarcoma" in this connection has been unwise; because of the inherent belief in the malignancy of sarcoma unnecessary mutilating operations have been performed.

Routine microscopic examination of tumor of the gum for corroboration of the clinical diagnosis is urged.

Dr. George Miller MacKee, of New York, directed the work represented in this paper. Dr. David L. Satenstein, or New York, assisted in the pathologic description of the lesion and the review of the literature.

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ZOSTERIFORM LICHEN PLANUS

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Since Devergie in 1854 first described linear lichen planus, numerous cases [1] have been reported in the literature, but there have been notably few of the more rare zosteriform lichen planus. Hence, a case recently presented before a combined meeting of the Chicago and the Detroit Dermatological Society is considered of sufficient interest to warrant description.

There is a definite distinction between the linear and the zosteriform type of lichen planus, to which there has not been strict adherence. In the former condition the papular elements appear as narrow lines not over 1 or 2 cm. wide, which may follow the course of a nerve, of a vein or of a lymphatic vessel or one of Voigt's lines. In the latter the lesions form a band several centimeters wide that follows the course of a peripheral cutaneous nerve and its branches or appears over areas of radicular nerve distribution.

REPORT OF A CASE

L. C., a 45 year old housewife, first noticed vague disturbances in the oral mucosa in August 1936. One month later she noted a small red patch just above the left flank. This was treated ineffectually with various topical applications. For several months the eruption continued to extend; there were some pruritus and burning. The patient stated that she had had an eruption in 1933 and another in 1934 in the same location; these were diagnosed as "shingles" by her physician. In the latter part of December the patient entered the clinic of the University Hospital.

The eruption was most marked on the abdomen and in the right lumbar region, with scattered lesions on the wrists and forearms and in the inguinal region. The predominating lesions were definitely zosteriform in their distribution and were made up of angular, flat-topped violaceous papules in which Wyckham's striae were evident. A linear band made up of these individual and confluent papules extended posteriorly from the region of the lower thoracic vertebrae and ran forward on the right side elliptically, reaching just below the costal margin at one point, and ending at the navel anteriorly. The band varied in width from less than a centimeter to several inches at its widest portion. This was approximately in the area of distribution of the eighth to the tenth thoracic nerve (figs. 1 and 2).

Examination of the mucous membranes showed several typical pearly lacy plaques along the buccal mucosa on either side.

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Studies and contributions from the Department of Dermatology and Syphilology, service of Dr. U. J. Wile, University of Michigan Medical School.

1. Auner, J. F.: J. Cutan. Dis. **25**:3, 1917.

The Kahn test was negative. The urine showed no albumin or sugar. No other essential abnormality was observed.

Fig. 1.—Anterior view of patient, showing zosteriform distribution of lesions in areas supplied by the eighth to tenth thoracic nerves.

Fig. 2.—Lateral view of patient, showing origin of the band at the spinal column. This band is composed of individual and confluent violaceous papules.

Histologic examination revealed the characteristic subpapillary lymphocytic infiltration of lichen planus (fig. 3).

On two previous occasions the patient had had an eruption (diagnosed as herpes zoster) in the areas involved at the time of my examination. The extreme rarity with which herpes zoster is known to recur makes it unlikely that both earlier eruptions were examples of this disease. It would seem more likely that the first eruption was herpes zoster, while the second manifestation was lichen planus. It would seem that the present lesions were a recurrence of the lichen planus at the locus minoris resistentiae produced by the previous herpes zoster.

Fig. 3.—Section, showing characteristic subpapillary lymphocytic infiltration.

COMMENT

Pinkus [1a] and later Ketron [2] considered the question of involvement of a cutaneous nerve in cases in which the lesions of lichen planus appear to follow its course.

Pinkus described zosteriform lichen planus in a woman. The eruption extended from the lateral and the posterior portion of the neck

1a. Pinkus, F.: Dermat. Ztschr. **12**:216, 1905.

2. Ketron, L.: Lichen Planus Linearis: Its Relation to a Cutaneous Nerve Experimentally Shown, Arch. Dermat. & Syph. **2**:358 (Sept.) 1920.

down over the shoulder to the anterior part of the chest in the midline, the region supplied by the fourth and the tenth spinal segment of the cord. Pinkus was unable to find any sensory changes or any evidence on pathologic examination of involvement of the small cutaneous nerve branches. He expressed the belief that it was highly unlikely that such widely separated segments of the cord (the fourth and the tenth) should be involved by the same process. He could find no evidence of involvement of either peripheral or central nerves and concluded that this particular regional distribution was evidence of the well known predisposition of certain areas of the skin to lichen planus.

Ketron [2] presented evidence that linear lichen planus definitely follows the course of a cutaneous nerve. In his case linear lichen planus followed a branch of the musculospiral nerve from the elbow to the middle of the index finger, coursing over the extensor surface of the forearm. He severed the nerve during the eruption, and anesthesia developed in an area along its course, 11 cm. distal to the severance, and lasted seven months. There was a temporary lessening of the pruritus, but the cutaneous lesion remained unchanged.

If the linear lichen planus is thus known to follow the course of a single cutaneous nerve, as shown by Ketron's work, it is reasonable to suppose that the segmental nerve distribution could be followed in zosteriform lichen planus.

The parallel between the distribution of zosteriform lichen planus and the areas of segmental nerve distribution has been observed in the classic cases of Fournier and Paris,[3] Balzer and Alquier [4] and Louste and associates.[5] More recently Jadassohn [6] cited Lang's case, in which there were zosteriform lesions of lichen planus on the thorax, associated with carcinomatous metastases to the spinal cord. This would seem to lend further support to the conception that some relation exists between the cutaneous nerves and zosteriform lichen planus.

SUMMARY

A case of zosteriform lichen planus is presented. The relation between lichen planus and the segmental nerve distribution is discussed.

3. Fournier, E., and Paris: Ann. de dermat. et syph. **2**:653, 1901.

4. Balzer, J., and Alquier, L.: Arch. gén. de méd. **5**:187, 1901.

5. Louste, Castel and Juster: Bull. Soc. franç. de dermat. et syph. **34**:851, 1927.

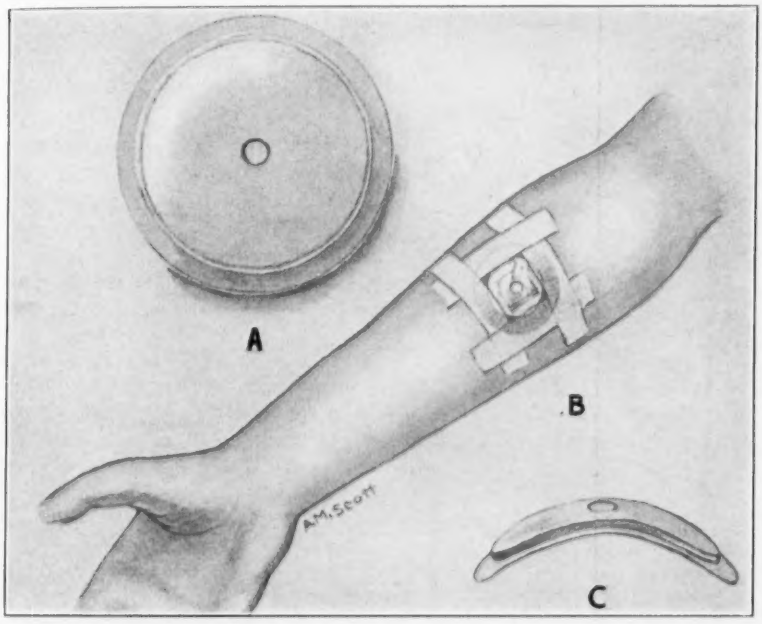
6. Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1931, vol. 7, pt. 2, p. 68.

Clinical Notes

A DEVICE FOR "CONTINUOUS" PATCH TESTS

HERBERT RATTNER, M.D., CHICAGO

Recently, I investigated the potential properties of a soap solution as a cutaneous irritant. The usual patch tests with the constituent materials of the solution were made on normal skins, and it was found, to my surprise, that the results were consistently negative. The gauze patches were then subjected to qualitative and quantitative chemical studies, and it was learned that the one suspected ingredient



Device for "continuous" patch test. *A* shows actual size; *B*, disk in use, and *C*, its flexibility.

was dissipated after a few hours, thus rendering valueless the ordinary twenty-four and forty-eight hour patch tests. It was necessary to devise some means of performing "continuous" patch tests, so that the test solution could be renewed at intervals to assure continuous contact with the skin. Various kinds of adhesive patches and ordinary shields used in vaccination were found to be impractical for study of a large group of cases; the celluloid disk shown in the sketch was tried and proved in every way suitable.

The device consists of a thin celluloid disk 2 inches (5 cm.) in diameter, with a small hole punched in the center, through which the solution can be inserted. The celluloid material is made of 0.010 acetate compound and is clear, transparent, free of camphor and flexible enough to conform to the arm. The disk has an outer

rim 1/8 inch (0.6 cm.) wide which rests on the skin. The inner portion is raised 1/32 inch (0.16 cm.) from the surface. This permits space enough for three or four layers of gauze, yet is sufficiently shallow to hold the patch in place. It was possible with this device to retain the patches on the skin for two weeks and more.

FULMINATING ACUTE LUPUS ERYTHEMATOSUS CURED BY SULFANILAMIDE

H. Ford Anderson, M.D., Washington, D. C.

Cases in which acute disseminated lupus erythematosus has been treated with sulfanilamide have not previously been reported, or at least my search of the literature has failed to reveal any.

When sulfanilamide therapy was instituted in the case to be described, the disease was of the fulminating type that usually terminates fatally in from a few hours to a few days.

REPORT OF A CASE

N. P., a married white woman aged 28, born in Georgia, was referred to me by Dr. Frank Hand on Jan. 5, 1937.

At that time typical discoid lupus erythematosus had been present for six years. About twelve atrophic areas, confined to the face, showed varying degrees of activity.

The patient had been under the care of several capable dermatologists, and her condition had improved to some extent after the administration of sodium gold thiosulfate and of a bismuth preparation. She then consulted a specialist in tuberculosis, and while she was under his care the lesions gradually became more active. Just before coming to Washington, D. C., she had submitted to complete examination including roentgen and laboratory studies at the Johns Hopkins Hospital. The report showed no evidence of tuberculosis or of an active focus of infection.

Instructions as to general hygiene, rest and extra diet were given, and small increasing doses of sodium gold thiosulfate were administered at weekly intervals. The dose was gradually increased to 100 mg., when a severe focal reaction together with a feeling of lassitude caused treatment to be discontinued.

When administration of the gold compound was resumed, it was noted that the maximum improvement was obtained by the use of a dose of about 30 mg. By the middle of August the activity of the lesions was approximately 25 per cent of what it had been in January.

When summer came she was warned against excessive exposure to sunlight. On Aug. 18, 1937, while giving her an injection, I observed a slight erythema on her shoulders and was told that she had been to the beach four days previously, that her erythema had been more marked but that it had faded, to such an extent that she had forgotten to tell me. The injection was immediately withdrawn, but not before she had received approximately 25 mg. of the 30 mg. dose.

On the night of her last injection, August 18, she became ill, with severe headache, sudden and complete prostration, articular and abdominal pains and fever. On August 19 her temperature was 103½ F. All the former symptoms were more pronounced, with distressing nausea and vomiting. On the face, the shoulders, the chest, the arms and the legs, in areas exactly coinciding with those exposed to the sun, there were lesions of varying sizes, the largest being that of a palm. They were edematous and of a dusky cyanotic hue. The sites of her old lupus erythematosus were fiery red and swollen.

From the Department of Dermatology and Syphilology, George Washington University.

Sodium thiosulfate was given intravenously, and general treatment for fever and administration of large amounts of fluid were employed.

On August 20 the patches on the sunburned area had coalesced and were sharply demarcated, while the areas protected by clothing remained comparatively white. The involved areas were edematous. All her symptoms were increasing. Her temperature was 104 F.

On August 21 the rash appeared more bluish, and there was a noticeable amount of small grayish and tightly adherent scales. The temperature was 105 F. She was taken to the Georgetown University Hospital, where a priest was summoned and she was prepared for a hasty death.

Tepid sponge baths, the application of wet sheets and subcutaneous administration of 1,000 cc. of saline solution, followed in six hours by 50 cc. of dextrose solution, were ordered. Fifteen grains (0.97 Gm.) of sulfanilamide was immediately given by mouth and retained. Administration of sulfanilamide in a dose of 15 grains (0.97 Gm.) every four hours to a total of 60 grains (3.88 Gm.) during the first twenty-four hours and in a dose of 10 grains (0.65 Gm.) every four hours to a total of 30 grains (1.94 Gm.) for the second twenty-four hours was then ordered.

In twenty-four hours the temperature had fallen to 98 F. It did not rise above normal again during her convalescence. The rash and the constitutional symptoms began to disappear within an hour after administration of the first dose of sulfanilamide. On August 24 she left the hospital, entirely free from symptoms, pigmentation of the involved areas alone remaining.

On Sept. 15, 1937, she was seen at my office. Not only had the pigmentation disappeared, but there was not the least sign of activity at the sites of the old discoid lupus erythematosus. By letter dated Feb. 15, 1938, she informed me that there still had been no recurrence. She had gained weight and felt better than she had for years.

SUMMARY

I have recorded a case of fulminating acute lupus erythematosus disseminatus, with apparent cure for six months after the use of sulfanilamide. In this case I believe a hidden streptococcic sepsis was at work. The process was precipitated by the use of sodium gold thiosulfate after undue exposure to the sun.

1746 K Street, N. W.

TREATMENT OF ERYTHEMA MULTIFORME EXSUDATIVUM WITH SULFANILAMIDE

Report of a Case

ALEXANDER BREGMAN, M.D., EDGEWATER, N. J.
Associate Dermatologist, Englewood Hospital, Englewood, N. J.

It is still unsettled whether the cause of erythema multiforme exsudativum is a toxemia or a microbic infection. The fact that in some cases reported in the literature streptococci have been suspected as the cause of this disease prompted me to try using sulfanilamide in a case of erythema multiforme which came under my observation.

REPORT OF CASE

R. W., a boy aged 14, was first seen by me on June 23, 1938. He stated that on June 21 he went swimming in a river. The following day he complained to his mother of general malaise, and on June 23 the eruption appeared. This consisted of flat-topped, disk-shaped papules, with a distinctly elevated and well defined marginal band; in some places these coalesced to form large circinate patches. They were pink or red and involved the face, neck, chest, back, buttocks, arms and legs. The oral mucosa was not involved. The patient complained of moderate itching. His temperature was 101.4 F. There was no history of previous ingestion of drugs or administration of serums.

Treatment.—The patient was ordered to bed and given a light diet. Sulfanilamide was then given in doses of 5 grains (0.32 Gm.) by mouth every two hours during waking hours. No other treatment, topical or systemic, was given at any time during the illness. The patient was seen again on June 25. The lesions appeared distinctly flatter and paler. The temperature was still 101 F., and his general condition was good. A total of twenty tablets had been given. Because of a severe headache, which I attributed to sulfanilamide, the drug was temporarily discontinued.

The patient was seen again on June 28. On that date only five or six lesions remained. They were widely scattered over the body and appeared even paler and more flattened. The temperature was 100 F. Since his headache had disappeared, sulfanilamide therapy was resumed and an additional fifteen tablets were given.

On July 1 the patient was seen for the last time. Not the slightest trace of the eruption was present, and the temperature was normal.

COMMENT

As spontaneous involution with complete recovery usually occurs in erythema multiforme exsudativum, it is difficult to evaluate the effect of any therapeutic measure in this condition. However, in a case of such extensive involvement one would expect the eruption to last a few weeks. The fact that the lesions began to fade and flatten forty-eight hours after the initiation of treatment with sulfanilamide and completely disappeared in eight days is suggestive of some therapeutic effect of this drug.

SUMMARY

A case of erythema multiforme exsudativum is reported in which sulfanilamide appeared to have a definite therapeutic effect.

News and Comment

AMERICAN ACADEMY OF DERMATOLOGY AND SYPHILOLGY

The first annual meeting of the American Academy of Dermatology and Syphilology will be held at the Hotel Jefferson in St. Louis on Nov. 14 and 15, 1938. The first day will be devoted to the educational program, which will consist of talks, half of them in one room and half in another simultaneously. During the luncheon hour there will be eight round table discussions on various subjects. The banquet will be held in the evening. On the second day there will be a clinic and a scientific exhibit. The discussion of the clinical cases will be held in the afternoon, after which there will be an executive session.

The speakers who will give the educational talks are Drs. George M. MacKee, New York; George W. McCoy, Washington, D. C.; George H. Belote, Ann Arbor, Mich.; Anthony C. Cipollaro, New York; Udo J. Wile, Ann Arbor, Mich.; F. E. Senear, Chicago; Charles C. Dennie, Kansas City, Mo.; H. N. Cole, Cleveland; George M. Lewis, New York; E. William Abramowitz, New York; Clark W. Finnerud, Chicago, and Karl G. Zwick, Cincinnati. Those who will conduct the round table discussions are Drs. Udo J. Wile, Ann Arbor, Mich.; Samuel M. Peck, New York; H. E. Michelson, Minneapolis; Louis A. Brunsting, Rochester, Minn.; H. R. Foerster, Milwaukee; W. H. Guy, Pittsburgh; Paul A. O'Leary, Rochester, Minn.

Further information may be obtained from the secretary, Dr. Earl D. Osborne, 471 Delaware Avenue, Buffalo.

ANNOUNCEMENT BY THE AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY

The written examination for certification by the board will be held Saturday, Oct. 15, 1938, in various cities.

The oral examination will be held on Friday and Saturday, Nov. 11 and 12, 1938, in St. Louis.

Further information may be obtained from the secretary, Dr. C. Guy Lane, 416 Marlborough Street, Boston.

Obituaries

JEAN DARIER, M.D.
1855-1938

When, after a long illness, Jean Darier died, on June 4, 1938, not only the group of his associates at the Hôpital Saint-Louis but the whole dermatosyphilologic world was made immeasurably poorer!

Darier was born in Budapest, Hungary, of parents whose ancestors had immigrated to Hungary from Dauphiné, France, after Louis XIV, king of France, revoked in 1685 the Edict of Nantes. As his parents had moved to the city of Geneva, Switzerland, Darier received his formal training in the basic sciences in that country. By 1876 he was a naturalized citizen of France, the fatherland of his forebears. After serving first as an *externe* in the clinics of Paris, he received an appointment as *interne des hôpitaux* in 1880.

It aids in understanding the range of Darier's research to bear in mind that his activity was influenced at first by his position of *répétiteur* in Ranvier's histologic institute of the Collège de France and later by his position as chief of the laboratory of pathologic anatomy of A. Fournier's clinic at the Hôpital Saint-Louis.

Darier's first publication registered the histologic observation, which was original with him, that the semilunar and auriculoventricular valves of the heart are normally without blood vessels. Darier was also the first to describe the nerve supply of lymph vessels. His thesis on diphtheritic bronchopneumonia, submitted for the degree of Doctor of Medicine, contained the first account in France of the isolation, cultivation and inoculation of the bacillus of diphtheria.

His collaboration with the celebrated syphilographer Fournier over ten years provided Darier with ample opportunities for studying in the clinic and in the laboratory the various phases and aspects of syphilis.

Darier described the histologic picture of cutaneous syphilid, of syphilitic arteritis, of gumma formation and of injuries to veins by arsphenamine and discussed the advantages and disadvantages of the old (mercurial) and the new (Ehrlich's arsenical) antisyphilitic remedies. As can be seen in the pages allotted to syphilis in the "Précis de dermatologie," his active interest in the subject did not cease after he left Fournier's department.

A list of twenty-four headings from the aforementioned work, which reads like the index of chapters in a treatise on dermatology and

syphilology, demonstrates more impressively than any words of mine could the comprehensiveness—one might justly say the catholicity—of Darier's activity in his chosen field.

Under the twenty-four headings he grouped approximately 250 publications, including only his writings published before 1928, the year of issue of the fourth edition of the "Précis"! The list is as follows and shows after each title (in parentheses) the number of articles under that title:

Généralités (11); érythèmes (3); eczéma et dermatoses érythémato-squameuses (5); érythrodermies (4); papules (4); dermatoses vésiculeuses, pustuleuses et bulleuses (6); kératoses (11); dyskératoses (19); dermatoses végétantes (9); nouures et sarcoïdes (13); ulcères et gangrènes (5); dyschromies (6); atrophies, scléroses, éléphantiasis (14); folliculoses, trichoses, etc. (11); dermites artificielles (7); prurigos (3); dermatoses parasitaires et dermatomycoses (6); tuberculose, tuberculides (24); lèpre (12); syphilis (23); tumeurs (21); épithéliomes (31); sarcomes, fibrosarcomes et melánosarcomes (7); thérapeutique (4).

The title "Généralités" includes, among other things, Darier's fundamental contributions to "La pratique dermatologique" on the anatomy and physiology of the skin, the general pathology of the skin and biopsy. The list of general articles includes also a publication on "The Histological Diagnosis of Dermatoses and Tumors of the Skin of Doubtful Character." This article appeared in the *Medical News* of Oct. 26, 1901, in New York.

A series of articles in the *Annales de dermatologie et de syphiligraphie* (1895-1896), critically reviewing Paul Gerson Unna's "Histopathologie der Hautkrankheiten," revealed that Darier kept himself informed on the scientific progress of dermatology in other countries.

That the practical aspects were not neglected by Darier may be gathered from his translation of Leo Leistikow's "Therapie der Hautkrankheiten," which was published in 1900 with additions from the pen of Darier.

Thanks, principally, to the efforts of Darier and his collaborators, the celebrated collection of moulages in the Hôpital Saint-Louis is now supplemented by a Musée d'histologie de l'Hôpital Saint-Louis which Darier and Civatte described before the Société française de dermatologie et syphiligraphie.

Exigencies of space permit me to refer only to some of the numerous path-finding investigations of Darier.

Among these must be mentioned *primo loco* the epidermal dystrophy first described (1889) by Darier under the name *psorospermose folliculaire végétante* but now familiar to every one as Darier's disease. The condition justly bears his name, since Darier's investigations contributed, as Jadassohn emphasized, much to the knowledge of this dyskeratosis. Darier himself was among the first to abandon the theory

of its infectious origin, according to which the morphologic alteration (dyskeratinization) was attributed to an invasion of the skin by the endoparasitic ameboid Sporozoa psorospermia.

The study of cutaneous cancer occupied Darier's attention from the beginning to the end of his scientific and practical activities.

From his first (1889) article on epithelioma of the sweat glands, more than one fifth of the total number of his writings in various journals and his reports at national and international conferences were devoted to the study of cutaneous cancer: its genesis, histology, classification, diagnosis, prognosis and treatment. With reference to treatment Darier insisted that the recognition of the type of cancer, by biopsy, should guide the decision as to the type of treatment, whether irradiation, excision in toto or electric cautery.

One of Darier's most significant and far reaching original contributions resulted from his investigations of the cutaneous manifestations of tuberculosis, in which he demonstrated two types of lesions, one being due to the invasion of the tissues by the active bacilli of Koch and the other (for which Darier coined the term *tuberculides*) being caused by the noxious substances (toxins, lipids, phosphatides and polysaccharides) produced by the bacilli. A discussion of the theoretic and practical import of the separation of the two types of lesions is out of place here, as every one is familiar with it.

In a continuation of his study of tuberculosis of the skin, Darier together with Roussy differentiated so-called sarcoid into the dermic form, known as Boeck's type, and the subcutaneous form, known as the Darier-Roussy type.

His investigations of the diseases caused by acid-fast bacilli included the study of leprosy, the results of which he embodied in reports to three international congresses, held in Berlin, Germany (1897), Bergen, Norway (1909), and Strasbourg, France (1923).

In a communication to the meeting in London, England, published in the Monatshefte für praktische Dermatologie (1896) Darier described pseudoxanthoma elasticum.

Darier was the first to discover that acanthosis nigricans of Pollitzer and Janovsky, previously described by Darier under the name "Dystrophie papillaire et pigmentaire" occurs frequently (in two thirds of the cases) in association with cancer of the abdominal viscera.

Darier's "Précis de dermatologie" is distinguished by several original characteristics. Its didactic merits appealed so generally to teachers of dermatology that it was translated into German, English and Spanish and—as Darier put it—"even imitated in the Japanese language." A second German edition has appeared recently.

Since I feel safe in assuming that all dermatologists are acquainted with Darier's more recent contributions, I shall refrain from enumerating them here. However, I cannot omit reference—at least briefly—to the interpretative exposition of the so-called *doctrine biologique* of Darier and his collaborators Tzanck and Civatte.

This doctrine aimed to supplement the purely static morphologic and one-sided etiologic explanations of cutaneous diseases by a biologic—i. e., dynamic—concept of their pathogenesis.

The doctrine, which Darier believed to be a most brilliant and fundamental advance in dermatology, was discussed at length by him and his two associates in the first volume of "Nouvelle pratique dermatologique," which is in the course of publication.

At the last (1935) International Congress of Dermatology, in Budapest, Hungary, Darier presented a most scholarly review of the history of dermatology. As I admire Darier's philosophic treatment of the past and his prophetic view of the future of dermatology, I recommend a perusal of this discourse to the dermatologic neophyte.

The greater number of Darier's publications considered here appeared under his name alone, but on many his name was joined with those of his teachers, associates and collaborators. Some of these were: Barthélemy, Chaillou, Civatte, de Christmas, Eliascheff, Ferrand, Fournier, Gautisier, Hallé, Hudelo, Jeanselme, Le Sourd, Oudin, Périn, Rist, Semon and Tzanck; numerous others deserve honorable mention in this connection.

As a practicing physician, Darier was a diagnostician of genius who recognized *prima vista* the essential pattern of a condition but supported and confirmed his intuitive conclusions by systematic study and meticulous observation.

In the preface to his "Précis de dermatologie" he formulated the principles which guided his activities:

> I have passed the greater part of my life in studying the diseases of the skin in the endeavor to develop for myself a personal conception of them. Whenever the attentive traditional scrutiny of the patient proved to be inadequate, I sought to obtain additional information by histologic analysis of biopsy specimens, by bacteriologic methods and by biologic reactions.

In surveying the scientific work of Darier one finds the record of an active, versatile, keenly analytic mind, responding to the influence of changing concepts and of new hypotheses and theories. His splendid life's work embraces, in addition, the documents of a whole series of methodical and painstaking investigations, the results of which were synthesized in original observations presented at the meetings of international congresses and published in the journals of Europe and America.

Darier stood out in the dermatologic world not only as an original scientific investigator but as an inspiring teacher who communicated and transmitted his encyclopedic learning without pedantry or ostentation.

That Darier's contributions to medical science were recognized and appreciated everywhere by his contemporaries is attested by the honors conferred on him.

Darier was an honorary member of all the principal dermatologic societies. He was the honorary president of the Société française de dermatologie and of the publication committee of the *Annales de dermatologie et de syphiligraphie.* He was a member of the Académie française de médecine and Commander of the Légion d'honneur.

The highest honor came to Darier at the International Dermatological Congress in his native city, Budapest, Hungary, when he was singled out from among dermatologic celebrities assembled from all over the world by the University of Hungary as the recipient of the honorary degree of doctor of medicine.

The ritual with which the degree was conferred was profoundly impressive, as it took place on the occasion of the ceremonial tercentenary celebration commemorating the founding of the university.

Darier's large bibliography, his authoritative textbook and the fine record of a whole generation of French dermatologists who were at some time under his tutelage speak in no uncertain terms of his rich and varied achievements, but they fail to reflect the intellectual and spiritual gifts which characterized his personality as a whole and endowed it with the charm that makes his death an irremediable loss to his friends.

Like nearly all great men, Darier was wonderfully good company; he laughed with one and smiled—inoffensively—at one. His familiarity with the idioms of several languages permitted him to spice his conversation with the Attic salt of humor in all of them. Darier was to the full the intellectual man of the world.

If there was one quality, however, more strongly developed in Darier than all others, it was his power of making friends. Where others made acquaintances, Darier made friends. He valued these friends, and it gave him sincere pleasure to meet them again and to keep in touch with them.

In addition to all his professional occupations, Darier took part in the civic administration of the community of Longpont, France, where he resided and where his simple funeral services were held.

The burial ceremony was attended by Sézary as representative of the Société française de dermatologie et de syphiligraphie; by Roussy, former dean of the Faculté de médecine de Paris and rector of the University, and by Achard, member of the Institute and representative of the Académie de médecine.

Many of Darier's colleagues and students from Paris and his fellow citizens from Longpont accompanied the body to its last resting place, near the village where he had lived during the last years of his long and fruitful life.

Milian, from whose tribute in *Paris Médical* were gathered the details about the last rites, concluded his article with the note that the coffin was hidden from view by the *roses d'adieu* deposited by the funeral cortège.

KARL G. ZWICK, Cincinnati.

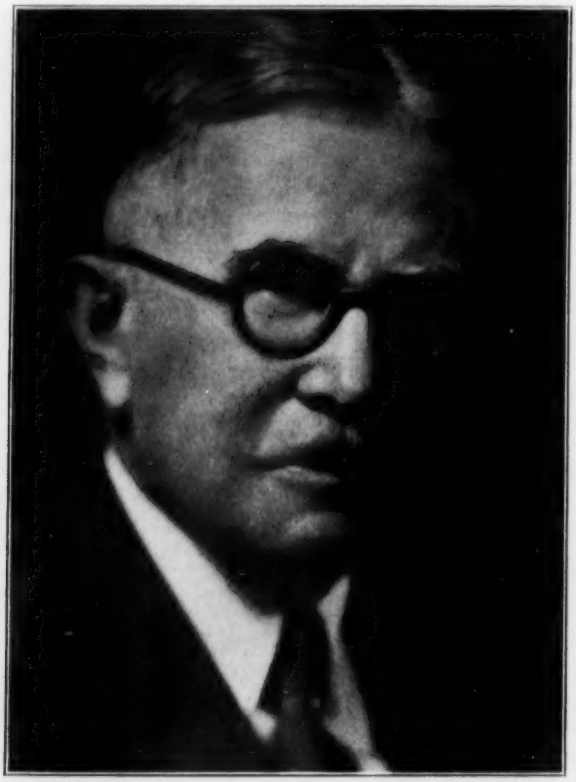
HENRY HOWARD WHITEHOUSE, M.D.
1864–1938

Henry Howard Whitehouse died at his summer home in Mystic, Conn., on Aug. 24, 1938. He was the son of Abraham Percival Whitehouse and Frances Deline Chaffee and was born in Hartford, Conn., on April 6, 1864. His father had been for many years superintendent of one of the departments of Colt's Patent Fire-Arms Manufacturing Company in Hartford and during the Civil War was chiefly instrumental in developing and improving the Gatling machine gun.

While a student at the Hartford High School, young Whitehouse won a Connecticut state scholarship, which enabled him to attend the Sheffield Scientific School at Yale University. He entered this institution in 1881 and graduated in 1885 with the degree of Ph.B. A year of special laboratory work with Prof. R. H. Chittenden followed, during which time various problems in physiologic chemistry were studied. In 1886 he matriculated at the Columbia University College of Physicians and Surgeons, from which he graduated in 1889.

After serving for a year and a half as resident physician at the Skin and Cancer Hospital he became associated with Dr. L. Duncan Bulkley in private and hospital practice. He also had close clinical association with Dr. George T. Elliot. A long dermatologic apprenticeship was served under Dr. Bulkley at the Skin and Cancer Hospital and under Dr. Elliot, first at the New York Post-Graduate Medical School and Hospital and later at Cornell University Medical College. From 1896 to 1909 he was chief of the class in cutaneous diseases at the Demilt Dispensary. His first major appointment came in 1911, when he succeeded Dr. George Henry Fox as attending physician at the Skin and Cancer Hospital. In 1921 he was elected president of the medical board and continued in that office until his resignation in 1928, when he was appointed consulting dermatologist. His loyal, unselfish service to the Skin and Cancer Hospital for thirty-eight consecutive years and his high sense of duty and responsibility furnished an example and inspiration to his associates. The opportunities for the study of clinical dermatology at this hospital were practically unlimited, and of them he availed himself to the fullest extent. His reward in professional experience was inestimable, but to the hospital he gave more than he received. Dr. Whitehouse was at one time consulting dermatologist to

the Manhattan State Hospital and from 1914 to 1925 professor of dermatology and syphilology and director of that department at the New York Post-Graduate Medical School and Hospital. He greatly enjoyed clinical teaching and was at his best when presenting cases to small groups of students. His lectures were carefully prepared and were so concise and interesting that they arrested and held the attention of even the casual matriculate.



HENRY HOWARD WHITEHOUSE, M.D.
1864-1938

Dr. Whitehouse was elected a member of the New York Dermatological Society in 1897 and of the American Dermatological Association in 1899. He served the former society as president for three different terms, and at the time of his death was the senior member. He was one of the original members of the Alumni Association of the Skin and Cancer Hospital, which he served first as secretary-treasurer, then as president and for a long time, until his death, again as secretary-treasurer.

Dr. Whitehouse did not write voluminously, but his contributions to the literature of dermatology were pertinent, scholarly and practical as well as scientific. He never wrote an article merely that he might be listed on some particular program, and he never wrote a line that was unnecessary to the logical presentation of his subject. Nor were his articles padded with irrelevant laboratory data or superfluous generalizations. Among some of his more important dermatologic studies may be mentioned the following: "A Case of Impetigo Herpetiformis (Hebra) in the Male," "Iodoform as an Internal Remedy in Lupus Erythematosus," "Xanthoma Multiplex: Histology of the Palmar Striae," "Liquid Air in Dermatology: Its Indications and Limitations," "Some Observations on the Results of the Wassermann Test in Scleroderma" and "Salvarsan and Neosalvarsan in Syphilis: A Comparative Study."

Whitehouse was, first of all, a physician, a brilliant diagnostician and a skilled therapeutist. Outside medicine, however, he had interests and recreations sufficiently diverse to balance and complement his professional work. He was a lover of good music, and of fishing even when it was not good. He was an ardent golfer and an excellent shot at the traps, but to him nothing in the way of outdoor activities could compare with the enjoyment that was his at sea with a hook and line.

Dr. Whitehouse was twice married, in 1893 to Lillian Van Winkle of Brooklyn, who died in 1930, and in 1932 to Carolyn Harding Beebe, the distinguished pianist and founder of the New York Chamber Music Society. She survives, as does a son by the first marriage, Irving Percival Whitehouse.

Henry Whitehouse had staunch friends among his dermatologic colleagues and the respect of all medical men with whom he came in contact. It is hoped that he also had the gratitude of some of the thousands of patients whose discomfort and suffering he relieved.

J. K.

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

INTRINSIC FACTORS IN THE ETIOLOGY OF NEOPLASMS. CARL V. WELLER, Am. J. Cancer **30**:39 (May) 1937.

Defining intrinsic factors as those inherent in the germ plasm, the author states that all organisms possess certain basic attributes essential for neoplastic growth. Neoplasms are considered to result from an interplay of intrinsic and extrinsic factors, and when the latter are sufficiently potent it is conceivable that a new growth may be induced in any organism.

SQUAMOUS-CELL EPITHELIOMA OF THE LEFT FOURTH FINGER: A CASE REPORT. H. SIGEL, Am. J. Cancer **30**:108 (May) 1937.

This case is reported because of the apparent rarity of epithelioma of the finger, only 2 cases having been recorded among 11,400 cases of cancer at the Bellevue Hospital. In 15 of the 22 cases reported in the literature there was a history of chronic irritation or of a preexisting benign lesion that had been frequently irritated by therapy or other means. FOERSTER, Milwaukee.

SCLEREDEMA ADULTORUM (BUSCHKE), WITH INVOLVEMENT OF THE MUSCLES IN AN ELEVEN YEAR OLD BOY. FRANK VERO and NICHOLAS E. PINGITORE, Am. J. Dis. Child. **54**:322 (Aug.) 1937.

A case of typical scleredema adultorum, a relatively rare condition, is described in an 11 year old boy. This followed an infectious disease (Vincent's angina or stomatitis). The literature is reviewed, with special reference to the occurrence of the disease in infants and children. The disease was of a mixed type, affecting the integument and the muscles, with consecutive limitation of motion of the head, the neck and the extremities, and was complicated by aspiration pneumonia apparently due to the involvement of the muscles of mastication and deglutition. Complete recovery took place within six weeks after the pneumonia.

DIETETIC TREATMENT OF ECZEMA IN INFANTS AND IN CHILDREN. H. FINKELSTEIN, Am. J. Dis. Child. **54**:344 (Aug.) 1937.

Finkelstein believes that in dealing with eczematous processes in children one must differentiate between seborrheic eczema and true eczema. Seborrheic eczema is a primary disturbance of the protein and fat metabolism in the skin, resulting in dyskeratosis with secondary inflammation. True eczema is a primary exudative inflammation with secondary dyskeratosis. In seborrheic eczema one finds a thick fatty crust on the scalp, and the disease shows a preference for regions which are exposed to maceration, particularly the genitocrural region, the armpits, the bends of the elbows, the folds of the neck in fat children and the folds at the beginning of the lobe of the ear. Blepharitis is a pathognomonic symptom of seborrheic eczema. The treatment of seborrheic eczema consists in the addition of from 10 to 15 Gm. of protein powder, such as calcium caseinate, and the use of skimmed milk or buttermilk; vitamin B_2 should be added to the diet. A large supply of carbohydrate should be included in the diet, but the fat content should be low.

True eczema, in contrast to seborrheic eczema, is a moist dermatitis accompanied with marked itching. If the moist element predominates, a wet or crusted eczema results. If this becomes secondarily infected, the condition is then impetiginous eczema. With little exudation and more desquamation, squamous eczema occurs. In the treatment of infantile eczema there should be a decided reduction

in the amount of milk, and only a small amount of carbohydrate is indicated. Sodium chloride should be eliminated. Finkelstein favors especially a diet of fruits, vegetables and carbohydrates but free from fats.

NELSON PAUL ANDERSON, Los Angeles.

SKIN IRRITATION AND CANCER IN THE U. S. NAVY. SIGISMUND PELLER and CHARLES S. STEPHENSON, Am. J. M. Sc. **194**:326 (Sept.) 1937.

Peller and Stephenson reviewed the statistics as to morbidity and mortality from cancer in the United States Navy. The mortality from cancer of the skin and the lip was about three times higher than among civilians of comparable ages. The morbidity was thought to be from seven and one-half to nine times higher than in the civil population.

Since the total morbidity and mortality from cancer in the navy is low, the authors believe that by exposing young men to strong cutaneous irritations which are not carcinogenous to inner organs, the lives of some who would die from internal cancer might be saved, at least for a certain number of years.

THERAPEUTIC VALUE OF CONVALESCENT SERUM IN SCARLET FEVER. MAX FOX and MAURICE HARDGROVE, Arch. Int. Med. **60**:494 (Sept.) 1937.

Fox and Hardgrove compare the results obtained of treatment in 139 cases of scarlet fever with commercial antitoxin and in 589 with pooled human serum of patients convalescent from scarlet fever with those in 300 cases in which neither medication was used but in which the general symptomatic treatment had been the same. The most satisfactory results were observed after the use of convalescent serum.

There was an apparent decrease in the mortality rate, as well as a reduction in the complications.

ELECTROLYTES OF BLOOD AND URINE OF DOGS WITH ACUTE HEPATIC INJURY PRODUCED BY ARSPHENAMINE. LOUIS J. SOFFER, D. A. DANTES and HARRY SOBOTKA, Arch. Int. Med. **60**:509 (Sept.) 1937.

Hepatic damage was produced in dogs by intravenous injection of arsphenamine in doses large enough to result in death of most of the animals. Chemical studies of the electrolytes of the blood are reported.

The most outstanding changes consisted of pronounced hemoconcentration, a drop in the chloride and the carbonate content and an increase in the inorganic phosphate and the lactic acid content of the serum. LYNCH, St. Paul.

SYPHILITIC EPILEPSY. W. L. BRUETSCH and M. A. BAHR, Am. J. Syph., Gonor. & Ven. Dis. **21**:255 (May) 1937.

The term syphilitic epilepsy is used to designate convulsive seizures which resemble idiopathic epilepsy in all respects and which leave no signs of organic disease of the brain. Differentiation from idiopathic epilepsy is often difficult and at times impossible during life. Anatomic examinations of brains of patients with syphilitic epilepsy are almost never performed. Five cases of syphilitic epilepsy are described. Four patients had multiple gross lesions in the cortex of the brain, due to syphilitic vascular disease. The fifth patient had microscopic areas of softening in the central convolutions, associated with syphilitic endarteritis of the cortical capillaries. The pathologic picture in all cases was characteristic of the meningovascular type of neurosyphilis.

SERUM CHOLESTEROL IN SYPHILIS. F. FERARU and F. OFFENKRANTZ, Am. J. Syph., Gonor. & Ven. Dis. **21**:267 (May) 1937.

Feraru and Offenkrantz conclude from their studies that the average amount of cholesterol in the serum is low in cases of early syphilis and that there is a gradual

rise as the disease progresses until in cases of tertiary syphilis the value is higher than the normal average. It is suggested that primary and secondary syphilis be regarded as manifestations of an acute infection and the tertiary stage as a degenerative process.

STUDIES IN CARDIOVASCULAR SYPHILIS: THE INCIDENCE OF SYPHILITIC AORTITIS. K. D. COCHEMS and J. E. KEMP, Am. J. Syph., Gonor. & Ven. Dis. **21**:282 (May) 1937.

In a study of 1,000 patients with syphilis of whom 92.6 per cent were white, there was aortic involvement in 12.7 per cent, the division among the various diagnostic categories of syphilitic aortic disease being as follows: aortitis 4.2 per cent; aortic insufficiency 2 per cent; aneurysm 4.7 per cent; aneurysm and aortic insufficiency combined 1.8 per cent. The incidence in female patients was 10.8 per cent and in male patients 13.4 per cent. The frequency of syphilitic aortic disease, and particularly of its more serious forms, increased equally with advancing years in male and in female patients. The recognition of syphilitic cardiovascular disease clinically is far behind the recognized incidence at necropsy.

SPINAL FLUID REACTION IN GENERAL PARESIS AS MODIFIED BY A COMBINATION OF THERAPEUTIC MALARIA AND TRYPARSAMIDE. L. MALETZ and H. C. SOLOMON, Am. J. Syph., Gonor. & Ven. Dis. **21**:287 (May) 1937.

Eighty-seven patients with dementia paralytica were given malaria therapy followed by administration of tryparsamide and studied especially for changes in the spinal fluid. The spinal fluid of these patients had been examined at intervals over periods of from two to ten years.

The cell count is usually quickly brought to normal, and at the end of a year is normal in 89 per cent of cases. The cell count, once having become normal, rarely rises above 6 cells per cubic millimeter again. The initial median cell count was 14 cells per cubic millimeter.

The figure for total protein drops quickly and reaches normal in one third of the cases at the end of one year. In many cases the figure remains well above normal even after five or more years. The higher the initial level, the smaller the likelihood that it will become normal.

The colloidal gold reaction is the least likely of the four criteria employed in this study to become negative. Only at the end of three years did half the patients show weak or negative reactions. At the end of five years none of the patients had strong gold curves.

The Wassermann reaction becomes weaker progressively and becomes negative in more cases with the lapse of time. At the end of one year 59 per cent of the patients had strong or moderately strong reactions, whereas in only 7 per cent was the reaction negative. After five years 37 per cent had completely negative and 30 per cent had strongly or moderately strongly positive reactions.

There appears to be no absolute relation in this group of cases between the clinical outcome and changes in the spinal fluid. The Wassermann, the colloidal gold or the total protein reaction of the spinal fluid remained positive in half of 21 cases studied ten years after malarial therapy.

POSTARSPHENAMINE JAUNDICE. L. J. SOFFER, Am. J. Syph., Gonor. & Ven. Dis. **21**:309 (May) 1937.

Soffer presents a careful statistical analysis of available clinical data concerning postarsphenamine jaundice.

Of a total of 18,250 patients receiving antisyphilitic treatment from 1919 to 1934 inclusive, 158 had jaundice, an incidence of 0.87 per cent. Arsphenamine caused jaundice one and a half times as frequently as neoarsphenamine. The stage of the disease during which the patient received treatment bore no relation to the frequency of postarsphenamine jaundice, nor did the total amount of the drug given. In 68 per cent of cases jaundice occurred during or after the completion

of the first ten intravenous arsenical treatments. In a little over half the cases jaundice appeared within ten days.

The role of heavy metal in the development of jaundice was difficult to determine. The clinical course of postarsphenamine jaundice was described. Malaise, nausea and vomiting were the most common symptoms, and these appeared from four to eight days before the appearance of icterus. Enlargement of the liver occurred in half the cases. In 7 instances the spleen was slightly enlarged, and ascites appeared in 4 cases. The presence of marked fever suggests either the development of arsphenamine dermatitis or the presence of an extensive necrotic process of the liver.

The duration of jaundice varied from ten to one hundred days. In 74 cases the icterus lasted from twenty-five to thirty-five days. In 81 cases further arsenical treatment was administered after jaundice had subsided, and of this group another attack of jaundice developed in 2.

Ten, or 6.3 per cent, of the 158 patients with arsenical hepatitis had acute yellow atrophy of the liver. Sixteen, or 10 per cent, had associated dermatitis.

Regarding the ultimate prognosis, the available evidence certainly suggests that long-continued use of arsenical compounds may produce progressive damage to the liver. It is believed entirely justifiable to assume that in the cases in which postarsenical icterus developed at some time or other evidence of impaired hepatic function may be found for many years after the jaundice has subsided.

THE VISCERAL PATHOLOGY IN HAITIAN TREPONEMATOSIS. C. V. WELLER, Am. J. Syph., Gonor. & Ven. Dis. **21**:357 (July) 1937.

This article is a supplemental report on the pathologic picture of Haitian treponematosis. The preceding article dealt with the pathologic picture of the aorta. This report deals with that of the heart, the adrenal glands, the liver, the pancreas, the brain and the meninges in a group of 174 autopsies from a specially selected group of Haitians among whom the incidence of scars and of a history of yaws was high. This study showed a high proportion of lesions in the viscera, as did the previous study in the aorta, which would be diagnosed as syphilitic in this country.

REUTER, Milwaukee.

MONOCYTIC LEUKEMIA: REPORT OF SIX CASES AND REVIEW OF ONE HUNDRED AND TWENTY-SEVEN CASES. EDWIN E. OSGOOD, Arch. Int. Med. **59**:931 (June) 1937.

Osgood believes that monocytic leukemia is more common than has previously been thought. The signs of this disease which are of particular interest to dermatologists are swelling of the gums (present in 80 per cent of cases), often associated with gangrenous stomatitis; petechiae (70 per cent), usually associated with bleeding from the mucous membranes, and enlargement of the lymph nodes (77 per cent), of the spleen (84 per cent) and of the liver (66 per cent). Pallor, weakness and fever are characteristic. Specific cutaneous nodules and pyoderma are frequently observed.

In 1 of the 6 cases reported by Osgood specific cutaneous lesions were present in the form of a maculopapular eruption. (There was a striking resemblance to erythema multiforme, a finding which I have described.—Abstracter.)

POISONING FROM CUTANOUS APPLICATION OF IODINE. W. B. SEYMOUR JR., Arch. Int. Med. **59**:952 (June) 1937.

Seymour reviews the manifestations of iodism, giving particular attention to the toxic symptoms following cutaneous application of ordinary tincture of iodine. Urticarial, pruritic and erythematous eruptions have previously been described. The author describes a case in which severe exfoliative dermatitis was observed and which terminated fatally.

The author quotes studies which suggest a relation between tuberculous infection and hypersensitivity to iodine.

LYNCH, St. Paul.

SULFANILAMIDE RASH. FRANCIS F. SCHWENTKER and SIDNEY GELMAN, Bull. Johns Hopkins Hosp. **61**:136 (Aug.) 1937.

Of 180 patients given sulfanilamide, an eruption developed in 10, or 6 per cent. The eruption was distinctly morbilliform and usually generalized. It appeared as early as the third day of medication; however, in half of the cases it appeared between the tenth and the fourteenth day. Fever and general malaise were always present and sometimes preceded the eruption by several hours. The temperature rose suddenly to from 101 to 103 F. and dropped to normal gradually. With the discontinuance of therapy the eruption rapidly faded and disappeared entirely in as short a time as forty-eight hours.

Readministration of sulfanilamide caused the rash to reappear faintly or in scattered areas, but it never assumed the former brilliance, and even this slight recrudescence gradually faded away.

If sulfanilamide therapy was not discontinued at the time of the appearance of the primary rash, the eruption faded and disappeared completely in about seventy-two hours.

NELSON PAUL ANDERSON, Los Angeles.

TRANSPLANTATION OF ADRENAL TISSUE IN ADDISON'S DISEASE. MAX A. GOLDZIEHER and S. B. BARISHAW, Endocrinology **21**:394 (May) 1937.

Goldzieher and Barishaw report a case of Addison's disease in which the patient was kept alive for eighteen months by administration of sodium chloride and extracts of adrenal cortex. Adrenal tissue obtained from a patient with hypercortical syndrome was then transplanted into the rectus muscle, and nine months of comparative good health resulted. Autopsy revealed survival of the transplanted tissue and complete atrophy of the patient's adrenal cortical tissue.

TREATMENT OF SEXUAL UNDERDEVELOPMENT WITH SYNTHETIC MALE HORMONE SUBSTANCE. JAMES B. HAMILTON, Endocrinology **21**:649 (Sept.) 1937.

A synthetic androgenic substance was administered to a 27 year old man suffering from hypogonadism, cryptorchidism, impotence and other manifestations of endocrine disturbance. After cessation of the first course of treatment acne developed but later disappeared. When the substance was again administered the acne recurred.

Hamilton states that a small group of boys complaining of severe acne during puberty have been treated with testosterone propionate, which caused disappearance of the acne, but he advises against drawing conclusions from these observations.

LYNCH, St. Paul.

SYPHILIS IN RELATION TO PREVENTION OF BLINDNESS: STUDY OF 100,000 CASE RECORDS. C. BERENS and J. A. GOLDBERG, J. A. M. A. **109**:777 (Sept. 4) 1937.

Berens and Goldberg report an analytic study of the records of 100,000 cases in an attempt to determine the incidence of syphilis in patients having diseases of the eye. They found that 5,969 patients (approximately 6 per cent) had ocular lesions in which syphilis may have been an etiologic factor. The Wassermann test had been made in only 37.5 per cent of their cases. In order to prevent sequelae, such as blindness, serologic tests should be made whenever there is any likelihood that the ocular condition is of syphilitic origin. The importance of accurate records of the family and the personal history and of systematic social service and follow-up work were stressed.

SKIN ERUPTIONS IN PATIENTS RECEIVING SULFANILAMIDE. J. G. MENVILLE and J. J. ARCHINARD, J. A. M. A. **109**:1008 (Sept. 25) 1937.

Menville and Archinard report 4 cases in which cutaneous reactions followed the ingestion of relatively large doses of sulfanilamide. The eruptions appeared

on skin exposed to sunlight. In each instance the rash was maculopapular and intensely pruritic, and in 1 case it was accompanied with chills, high fever and prostration. When medication was stopped, prompt recovery occurred in all cases.

DEVELOPMENT OF CUTANEOUS ERUPTION (TOXICODERMATOSIS) DURING ADMINISTRATION OF SULFANILAMIDE: REPORT OF TWO CASES. M. H. GOODMAN and C. S. LEVY, J. A. M. A. **109**:1009 (Sept. 25) 1937.

In 2 cases of cutaneous eruption reported by Goodman and Levy as instances of reaction to ingestion of sulfanilamide, there was a similarity in the parts involved, the presence of itching, the character of the lesions and the presence of systemic toxic symptoms. The parts affected included the face, the neck, the shoulders, the occipital area of the scalp and the arms, where the lesions were more numerous on the extensor than on the flexor aspects. The lesions were discrete rounded reddish macules and papules of varying sizes. In 1 case a few purpuric spots were noted. No mention was made of exposure to sunlight. Patch, scratch and intradermal tests with sulfanilamide were carried out. One patient reacted positively to the scratch test. The other tests gave negative responses.

DERMATITIS FROM SULFANILAMIDE. L. J. FRANK, J. A. M. A. **109**:1011 (Sept. 25) 1937.

Frank noted that in 2 men exposure to the sun following the ingestion of sulfanilamide resulted in an eruption of the multiform erythema type. The lesions were more pronounced on the sites exposed to the ultraviolet rays but later spread to covered portions of the body as well. Diffuse erythema, edema and severe itching were noted in both patients.

NEW YORK CITY PLAN FOR COMBATING SYPHILIS. C. W. CLARKE, J. A. M. A. **109**:1021 (Sept. 25) 1937.

The department of health of the city of New York maintains seventeen diagnostic centers where specimens of blood are taken, dark field examinations are performed and diagnostic consultations are available. According to Clarke, 345,000 serologic tests for syphilis were performed without charge during 1936. Drugs for the treatment of early syphilis, syphilis in pregnancy and congenital syphilis are suppled free on request of the physician. Specially trained physicians are avaialble to assist in tracing the source of the infection and in the examination of persons with whom the patient has come in contact. A pamphlet giving information about the infection and how to protect persons with whom they come in contact is provided for distribution to all patients with syphilis. Postgraduate instruction in accepted modern methods of diagnosis and treatment are made available to physicians. The reporting of cases of syphilis is facilitated for the private practitioner by the provision of suitable and convenient forms. To many of the clinics of the voluntary hospitals free drugs are supplied. There is a shortage of beds for isolation of patients with infectious syphilis. The department of health has the right to detain forcibly a person with infectious syphilis when such action is determined best. Ten centers for treatment are maintained by the board of health. From 60 to 90 per cent of the patients attending these clinics are on some form of unemployment relief. Clarke considers the instruction of the public with regard to syphilis an important function of the department of health. This is undertaken in cooperation with the press, the radio and voluntary societies. The number of reported cases of syphilis has increased 50 per cent, from 42,315 in 1932 to 67,010 in 1936. LEWIS, New York.

A CASE OF LIPOPHAGIC GRANULOMA AND SCLEREMA NEONATORUM. F. J. EICHENLAUB and I. L. SANDLER, South. M. J. **30**:527 (May) 1937.

The authors present a case of combined lipophagic granuloma and sclerema neonatorum. The granuloma developed first and was diagnosed as subcutaneous

fat necrosis by biopsy. The second disease developed after otitis media and probable bronchopneumonia caused inanition and dehydration. While the patient was in this state, true sclerema neonatorum developed. The authors believe this to be the first instance in which the conditions occurred simultaneously in the same patient.

SCHLUTZ, Chicago. [AM. J. DIS. CHILD.]

INDUSTRIAL DERMATITIS AND THE WORKMEN'S COMPENSATION ACT. H. MAC CORMAC, Brit. J. Dermat. **49**:409 (Oct.) 1937. INDUSTRIAL DERMATITIS AND THE WORKMEN'S COMPENSATION ACT. R. D. GILLESPIE, ibid. **49**:422 (Oct.) 1937. INDUSTRIAL DERMATITIS FROM THE LEGAL STANDPOINT. ERSKINE HILL, ibid. **49**:427 (Oct.) 1937.

These were the opening papers in a symposium on industrial dermatitis and the Workmen's Compensation Act, a problem that "bristles with difficulties." MacCormac suggested that in may cases in which the condition is thought to be due to occupation it is, in fact, idiopathic eczema developing in a workman—particularly in those cases in which the disease develops in workmen past middle age and in which the eruption is persistent and then spreads to other parts of the body to become generalized. The distinguishing clinical features of genuine occupational dermatitis are that they appear abruptly and that the patient recovers in a reasonable time when contact with the irritant ceases. The author rejected the hypothesis of autosensitization and expressed the belief that patch tests are unreliable.

Gillespie's paper deals with the influence of psychogenic factors in the production of occupational dermatitis, citing examples in which frustrated ambition or distaste for one's job for one reason or another led to the development of industrial neurosis. Such a complex, he stated, increases the proneness to dermatitis arising from industrial irritants. He suggested that perhaps MacCormac's middle-aged workmen were becoming "afraid of their jobs"—i. e., afraid of unfitness and consequent loss of employment.

Hill dealt with the purely legal problems of the British Industrial Workmen's Compensation Act. The papers stimulated an interesting discussion, there being some adherents but more opponents to the theories of the essayists.

STUDIES OF PHOTOSENSITIZATION BY PORPHYRINS. H. F. BLUM and N. PACE, Brit. J. Dermat. **49**:465 (Nov.) 1937.

"The destructive skin-lesions of hydroa vacciniforme seu aestivale are generally attributed to the photosensitizing action of porphyrins, since porphyrinuria is a common accompaniment of this disease. However, although numerous attempts have been made to reproduce the lesions of hydroa by exposure to light, a great deal of uncertainty surrounds such studies, and a definite step in the proof of their aetiology is lacking. Undoubtedly part of the difficulty lies in . . . the tacit assumption that all cases of abnormal sensitivity to light have a common aetiology —an assumption which is . . . untenable . . . Further difficulty lies in the failure to consider the character of light sources and the photophysiology of the skin, and it is to these phases of the problem that this paper is devoted."

The authors describe and discuss their experiments, the results of which they summarize as follows:

"The absorption spectrum of porphyrins indicates that their spectral region of greatest photosensitizing activity should lie in the near ultraviolet and violet between 3300 and 4300 Å, but that they should also sensitize in the visible.

"Studies using different sources and filters show that the photosensitizing activity of haematoporphyrin for normal skin corresponds approximately with its absorption spectrum.

"Studies of a case of hydroa vacciniforme with porphyrinuria failed to demonstrate that the lesions of this disease are produced by the wavelengths to which porphyrins sensitize the skin.

"Repeated exposure to the radiations which elicit sunburn in normal skin failed to reproduce the hydroa lesions."

LIPSTICK DERMATITIS, WITH REPORT OF CASE DUE TO EOSIN. F. F. HELLIER, Brit. J. Dermat. **49**:485 (Nov.) 1937.

Hellier reports in detail a case of lipstick dermatitis which by patch tests he proved to be due to eosin. In another case he found the dermatitis to be due to some ingredient other than eosin. In general, the ingredients of lipstick may be divided into three groups: those of the base, those of the perfume and those of the coloring matter. In most cases cheilitis is caused by the perfume or the coloring matter. Hellier discusses the possible effect of sunlight in cases in which the disease is due to eosin. The pertinent literature is reviewed.

RATTNER, Chicago.

LUETIC PSEUDO-CYSTICERCOSIS. A. CASTELLANI, J. Trop. Med. **40**:232 (Oct. 1) 1937.

The author gives a brief account of a syphilitic condition thought not to have been previously described. The lesions are small subcutaneous nodules on the arms and the legs which are discovered by palpation rather than by inspection. They are about the size of grains of rice and are not tender. The author observed 3 cases of such an involvement, in 2 of which the condition had been previously diagnosed as cysticercosis. In all instances strongly positive Wassermann reactions were obtained. Histologic sections showed that the nodules consisted of fibrous tissue. The lesions responded to antisyphilitic therapy.

CUTANEOUS MANIFESTATIONS OF MYELOGENOUS LEUKEMIA. LOUIS NÉKAM, Bull. Soc. franç. de dermat. et syph. **44**:1236 (July) 1937.

Nékam considers in great detail the cutaneous findings in cases of chronic myelogenous leukemia. In forty-two years, 44 published cases in which this blood dyscrasia was accompanied with lesions of the skin were collected. In 25 the diagnosis seemed unquestionable, and of this number histologic study was made in 18. In 18 of the 25 cases there was cutaneous tumor, in 4 leukemid, in 1 erythroderma, in 1 a bullous eruption and in 1 a rosaceaform exanthem with specific structure.

BENIGN LYMPHADENOID GRANULOMA. G. MIESCHER, Bull. Soc. franç. de dermat. et syph. **44**:1254 (July) 1937.

The author calls attention to a granulomatous lymphadenoid disease generally called lymphocytoma. The first case was presented by J. Jadassohn in 1906. In that case a patient aged 33 had brownish red papules on the cheeks. Healing resulted from prolonged use of arsenic. The dermatosis was termed pseudoleukemia of the skin by Jadassohn, on account of the absence of changes in the blood and the lack of involvement of the lymph nodes.

Lymphadenoid granuloma is characterized by papulonodules of various dimensions, often symmetrically situated. The color is red, brown or violet, and the surface of the lesions is smooth. The evolution is extremely slow. The localization is usually on the face, the lobes of the ears or the scrotum. Involvement of the extremities is rare. The general health of the patient is not changed; the spleen and the lymph nodes are not enlarged, and the blood picture is normal except for occasional mild lymphocytosis (30 or 40 per cent). The disease can appear at any time from infancy to old age and favors feminine subjects. Favorable results are obtained with arsenical therapy and roentgen irradiation.

The histologic variations are uniform and consist of round or oval nodular intradermal infiltrations, usually well demarcated. The cells are distinctly lymphadenoid, chiefly small lymphocytes, and the infiltrations assume the formation of lymphatic follicles, a feature which is characteristic. The disease is one sui generis and, according to Miescher, should be given the name benign lymphadenoid rather than lymphocytoma.

A Case of Dermolipodystrophy. Hufnagel, Bull. Soc. franç. de dermat. et syph. **44**:1665 (July) 1937.

The author described an unusual case of atrophy of the skin and subcutaneous adipose tissue in a woman, whose age is not stated. Only the head, the neck, the arms and the upper part of the trunk were affected. The picture resembled that condition described as lipodystrophy by Simons in 1911. Histologic sections in Hufnagel's case showed inflammation of the blood vessels, sclerosis and an inflammatory infiltrate involving the cutis and the hypoderm but respecting the epidermis. Civatte expressed the belief that the histologic features of this disease are analogous to those of erythromelia but with much less infiltrate and more marked sclerosis. The patient had both neurosyphilis and Hodgkin's disease, although the etiologic relation of these diseases to the cutaneous condition could not be exactly determined.

Laymon, Minneapolis.

Report on Helminthiasis and Dermatoses. E. Cappelli, Dermosifilografo **16**:508 (Dec.) 1937.

The role that intestinal parasites play in certain dermatoses is discussed in this preliminary communication. The cutaneous lesions for the most part are diffuse and generalized. The elementary lesion is usually a small pruriginous and conical papule, of bright or dark red, which is covered by a blood crust. Sometimes the lesions are vesicular, and in some cases the condition resembles neurodermatitis.

The relation of dermatoses to intestinal parasites is infrequently recognized. Even asthma can be caused by intestinal worms. The author points out many interesting problems that need to be worked out before this whole subject is clarified. Some of these are: (1) the epidemiologic aspects, (2) the frequency of infestation, (3) the cutaneous morbidity in respect to the presence of intestinal parasites, (4) the number and kind of worms, their localization in the intestinal tract and their influence on the severity of the dermatoses they produce, (5) immunologic aspects and (6) their effect on general health, anemia, eosinophilia, etc.

Cipollaro, New York.

Stenosing Proctitis and Nicolas-Favre's Disease. Jorge R. Muñiz, Vida nueva **15**:178 (Sept. 15) 1937.

The author has studied 40 cases of rectal stricture which he attributes to lymphogranuloma venereum, although the Frei test was positive in only 35. Of the group studied 28 patients were female and 12 male; 28 were of pure Negro or mixed race and 12 white. The author feels that some of the 12 white subjects may have had a small admixture of Negro blood. The age of the patients varied from 23 to 57 years. In only 8 of the 40 cases were there positive Wassermann and Kahn reactions. In 90 per cent of cases the stricture was palpable digitally; it was never complete, the smallest orifice found being 1 cm. in diameter. Anal ulceration, secondary pyogenic infection and sinuses were noted frequently. Contrary to general opinion, he found the suprastenotic colon often in a practically normal state. Antimony salts have been effective in clearing up ulcers, inflammations and suppurations but have not influenced the stricture. Frei antigen intravenously gave slight febrile response and totally disappointing therapeutic

effects. He feels the best therapy for the stricture is slow, progressive and repeated dilatation and has kept patients well and comfortable for years by this method. In cases in which the outlook is hopeless radical operation with preliminary colostomy and subsequent proctectomy must be done.

LEIFER, New York.

ULCUS VULVAE ACUTUM WITH ULCERS IN MOUTH. H. TAGAMI, Jap. J. Dermat. & Urol. **42**:277 (Nov.) 1937.

The author reports 2 cases of ulcus vulvae acutum associated with similar ulcerations in the mouth, in which he made histologic examination. In 1 case the eruption appeared soon after menstruation and disappeared before the next menstrual period. In all the lesions numerous thick gram-positive bacilli were demonstrated and cultured. Experimental inoculation of human beings and animals, however, produced negative results. Both patients were sensitive to epinephrine.

PEPSIN OF SERUM IN EXPERIMENTAL DERMATITIS. K. YOSHIOKA, Jap. J. Dermat. & Urol. **42**:278 (Nov.) 1937.

The author produced artificial dermatitis in the rabbit and determined at certain intervals the nonprotein nitrogen and the pepsin content of the serum. He found a marked decrease in pepsin at the height of the dermatitis and a gradual return to normal during the period of healing. The nonprotein nitrogen content was slightly increased at the height of the dermatitis.

SUPERINFECTION OF SYPHILIS IN MAN. T. AKIMA, Jap. J. Dermat. & Urol. **42**: 294 (Nov.) 1937.

The author inoculated 55 patients with syphilis in all stages and produced superinfection in 29. The older the syphilitic infection was, the less successful was the superinfection. Twenty-eight of the 29 successful inoculations produced an infiltrated papule which histologically showed syphilitic structure. In 1 case infiltrated ulcers with the histologic structure of a primary syphilitic lesion were obtained. In 3 of 8 cases of dementia paralytica a necrotic ulcer developed after inoculation of syphilitic material. In 1 case a pea-sized copper-colored markedly infiltrated papule containing Spirochaeta pallida developed.

The lesions produced by inoculation were not always of the same stage as the patient's disease. In 1 case of primary syphilis the appearance of the secondary eruption was accelerated by the superinfection. Among 16 cases of successful inoculation in which the complement fixation reaction was determined, an increase in the titer was observed in 12. Among 21 cases of unsuccessful inoculation in only 6 was a similar change noted. No difference was noted in the effect of therapy between cases in which inoculation was successful and those in which it was unsuccessful.

BLOOM, New York.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

THOMAS W. NISBET, M.D., *Chairman*

March 8, 1938

CHARLES R. CASKEY, M.D., *Secretary*

Lupus Vulgaris (Hypertrophic). Presented by DR. STANLEY CHAMBERS, DR. STANLEY ANDERSON and DR. M. NORRIS ROSENBERG.

M. Y., a white man aged 39, has had chronic pulmonary tuberculosis (arrested) for several years. He first had trouble in the anal region about twenty years ago. At that time several operations were performed for fistula in ano. After these the skin remained thickened. At present there is on the left buttock, extending from the median line and the region of the anal mucosa laterally, a large area of cutaneous hypertrophy approximately 3 by 6 inches (8 by 15 cm.). The surface appears edematous and granulomatous, with slight exudation and crusting. On the borders are small ulcerations from which pus can be expressed. The patient's sputum and a direct smear from the tissue showed no tubercle bacilli. The Wassermann reaction was negative. The histologic examination showed marked cellular infiltration of the entire corium. Most of the cells were lymphocytes, but many plasma cells were present. In many places there were tubercles and giant cells. There was no caseation. The diagnosis was granuloma, probably tuberculous.

DISCUSSION

DR. H. C. L. LINDSAY: One part of the lesion has become keloidal. The lesion looks more like blastomycosis than lupus vulgaris. It would be advisable to take more specimens and look for blastomycetes microscopically. In tuberculous lesions covering 5 square inches (32 sq. cm.) one would expect tubercles to break out in the areas of scarring.

DR. SAUL S. ROBINSON: I recently had a patient with similar lesions, which were diagnosed as hypertrophic lupus vulgaris. Eventually the diagnosis was changed to blastomycosis. Small pustules appeared on the margin; these showed blastomycetes. I should suggest a therapeutic test with iodides.

DR. JULIUS R. SCHOLTZ: I think that, as the patient has far advanced fibroid pulmonary tuberculosis, therapeutic use of iodides is contraindicated.

DR. NELSON PAUL ANDERSON: Tuberculous lesions of the skin no larger than a dollar should be excised. I do not believe any one will cure this large plaque by radiotherapy. I recommend excision. I think that if this had been done from three to five years ago, when the patient had the original smaller plaque, cure would have been obtained.

A Case for Diagnosis (Keloid?). Presented by DR. NELSON PAUL ANDERSON.

D. C., a white boy aged 11 years, has had an infiltrated hard tumor the size of a large bean on the right shoulder for one year. There is no history of injury. A roentgenogram failed to disclose any foreign object.

DISCUSSION

DR. H. S. CAMPBELL: I think the lesion is a keloid that has suffered superficial injury, as it has a small scab on its surface. A small nick in the surface previous to therapy would be enough evidence to justify histologic diagnosis. I find that small circumscribed keloids, as exemplified by those occasionally

following vaccination, undergo involution only inconstantly under the influence of roentgen rays, whereas they always respond to freezing. Some lesions may require several freezing treatments. The adjoining skin should be protected by blotting paper in which an opening has been cut to fit the lesion.

DR. SAMUEL AYRES JR.: I think the lesion is an example of subepidermal fibrosis of Michelson. Some of the lesions are on the legs and some on the arms. A patient at the Los Angeles County Hospital several years ago had similar multiple lesions which histologically belonged in the same category. As far as treatment is concerned, either freezing or roentgen irradiation would be of value. I observed a case in which the condition practically subsided during roentgen irradiation and I think the fact that this condition has been present less than one year would make the outlook favorable for such treatment.

Localized Argyria Following Treatment of Burn with Tannic Acid and Silver Nitrate. Presented by DR. SAMUEL AYRES JR.

D. O., a white girl aged 3 years, was burned on the right thigh with hot coffee three months ago. The burn was said to be of moderate severity. It was treated by the tannic acid–silver nitrate method almost immediately. At this time she presents on the left thigh and buttocks several extensive, relatively superficial scars. One of these shows slight keloid formation. Most of the areas show a deep slate gray pigmentation. This patient has been presented for several reasons. The physician who treated her is concerned because the parents are threatening a lawsuit on account of the pigmentation. The method of treating burns with tannic acid and silver nitrate was introduced by A. G. Bettman (*Northwest Med.* **34**:46 [Feb.] 1935). It consists of applying, by spray or applicator, 5 per cent tannic acid and then daubing on 10 per cent silver nitrate. A thick eschar forms; this dries and in several weeks separates and leaves a soft cicatrix. The technic is applicable chiefly in deep burns. In reference to this treatment M. B. Low (*New England J. Med.* **216**:553 [April 1] 1937) said:

"The local area should be cleansed gently and speedily with a mixture of green soap and peroxide, followed by a solution of 70 per cent alcohol or hexylresorcinol. . . . Following cleansing, we apply a fresh 5 per cent tannic acid solution to the burned areas and, immediately afterwards, sop on a solution of 10 per cent silver nitrate. . . .

"We have continued to be impressed with the excellence of the tannic acid–silver nitrate treatment of burns. . . . We have considered the dangers of argyria but have not seen any cases resulting from the use of silver in this way, and would not expect to encounter any for the following reasons: there is only one application, there is very little absorption from the burned area, especially with the formation of an immediate eschar, and the silver is not in organic or colloidal combination."

A. G. Bettman (*J. A. M. A.* **108**:1490 [May 1] 1937) said: "That no absorption of silver takes place even when extremely large amounts of solution are used is proved by the fact that in none of the many cases treated has argyria or other evidences of silver absorption been seen, although carefully watched for. It has not been noted by other surgeons who have reported experience with this treatment."

DISCUSSION

DR. SAMUEL AYRES JR.: In view of that evidence, it appears that this case is exceptional. The child was burned with hot coffee spilled on it. Within five minutes the wound was cleansed and treated with tannic acid and silver nitrate. When the eschar came away, this slate gray pigmentation was left. I should be interested in knowing if other members have heard of argyria following this treatment. The parents are anxious to get rid of the pigment, and I expect to use the method suggested by A. W. Stillians and T. K. Lawless (*J. A. M. A.* **92**:20 [Jan. 5] 1929) for the removal of the silver deposit, which consists of subcutaneous injection of sodium thiosulfate and potassium ferricyanide in distilled water.

Dermatophytosis (Hands, Feet and Toe Nails) Due to Trichophyton Purpureum. Presented by DR. NELSON PAUL ANDERSON.

F. C. T., a white man aged 27, was first seen Jan. 11, 1937. At that time he had an eruption on the left hand of five years' duration, which apparently had started in a cut. "Water blisters" appeared, and the condition gradually spread to involve the palm and the fingers. The skin becomes better at times but is never entirely free from evidence of the disease. There has been occasional trouble with an eruption on the toes and feet. The right hand is normal. The left hand presents a slight diffuse erythema, with many areas of scaling. The feet show definite evidence of dermatophytosis and the left first, fourth and fifth toe nails show evidence of infection beneath the free edges. Treatment has consisted of application of small doses of unfiltered roentgen rays, compound ointment of benzoic acid and crude coal tar paste. It has been without effect.

This condition is due to infection by Trichophyton purpureum. Mycelia have been seen under the microscope. Conditions of this type are interesting because of the involvement of one hand and resistance to therapy.

DISCUSSION

DR. C. R. HALLORAN: This condition is dermatophytosis of the hands and feet. True dermatophytosis of the hands and feet is not to be confused with psoriasis of the same areas, although in that condition it may be possible to demonstrate fungi. It is readily understandable that a secondary fungous infection may often be found in cases of psoriasis of the hands and feet.

DR. NELSON PAUL ANDERSON: I should like to bring this patient and the 2 presented by Dr. Ayres at the December meeting of the society (ARCH. DERMAT. & SYPH. **37**:1066 [June] 1938) before the society and place them behind a dark curtain with only their hands projecting. With such a method of presentation, I am sure Dr. Halloran would find it difficult to differentiate this patient from the ones presented by Dr. Ayres. The patient has been under observation for over a year. The condition has not changed in the slightest, either with or without treatment.

DR. SAMUEL AYRES JR.: Fungi may be observed not only on the feet but on the hands. At every examination scales may be picked off at will and be found loaded with mycelia. Every time the patient comes for observation the organism can be demonstrated.

Cellulitis of Neck Following Acne (Hemolytic Staphylococcus). Presented by DR. H. C. L. LINDSAY.

THOMAS W. NISBET, M.D., *Chairman*

April 12, 1938

CHARLES R. CASKEY, M.D., *Secretary*

Tuberculous Chancre. Presented by DR. MAX J. WOLFF.

C. B., a man aged 27, had a lesion on the right elbow for six months. It began with what he thought was a boil. There was a discharge of pus which never healed completely. The lesion remained the same size for four months, after which a lump developed in the right axilla. This at first was firm and hard but in the past few weeks has showed signs of fluctuation. The Wassermann reaction was negative. Histologic examination of the lesion on the elbow showed numerous collections of epithelioid cells, with an occasional giant cell of the

Langhans type and a dense infiltration of lymphocytes. The Mantoux test gave a negative result and the agglutination test for tularemia a negative result.

DISCUSSION

DR. HARRY P. JACOBSON: It is likely that the presenter's diagnosis is correct. However, sporotrichosis deserves consideration. To all appearances, this patient is in good health generally and shows no systemic reaction, and the lesion is of six months' duration. I should suggest an attempt to secure pus from the unopened involved gland and its microscopic and cultural study to exclude or establish the diagnosis of sporotrichosis. I might also suggest that several culture tubes be inoculated at room and at incubator temperature.

DR. C. R. ANDERSON: In sporotrichosis one would find large nodes and draining sinuses along the lymphatic channels. In this case there are pipestem lymphangitis and axillary adenopathy. The ulcer on the elbow is typical of tuberculous chancre in that miliary apple jelly nodules are seen in the periphery of the lesion. I agree with the diagnosis as presented.

DR. H. C. L. LINDSAY: At San Diego, Calif., in May 1936, at a meeting of the Dermatology and Syphilology Section of the California State Medical Society, I read a paper which was strongly criticized by Dr. Howard Morrow because of the use of the word "chancre"—i. e., tuberculous chancre. I notice today in the literature that "tuberculous chancre" is used a great deal.

DR. SAMUEL AYRES JR.: I think this case is difficult. When I quizzed this patient rather closely, he said the lesion originally began as a boil. There was a discharge of pus followed by an ascending lymphangitis on his arm and an enlarged gland in the axilla. The enlargement of the gland then subsided, but the lesion at the elbow persisted, and after a month or two the glands under the arm again became swollen. There certainly must have been an element of pyoderma to account for the immediate enlargement of the axillary gland. I should say that this condition may be a pyogenic infection which gives a granulomatous picture with lymphadenitis.

DR. H. C. L. LINDSAY: I should suggest that pus be withdrawn from the axillary gland and a guinea pig inoculated with it.

DR. MAX J. WOLFF: I feel that the roentgen findings in the chest were important. There was no evidence of calcified lymph glands and no other evidence of tuberculous infection.

A Case for Diagnosis (Syphilis?) (Mycosis Fungoides?). Presented by DR. IRVING R. BANCROFT.

V. F. E., a white man aged 64, states that fifteen years ago small macules appeared scattered over the body. These disappeared but returned after a few years and gradually grew larger. At present he shows a number of palm-sized sharply marginated red patches on the trunk. On the right side of the neck is a granulomatous lesion, slightly ulcerated at the apex. Over the right eye there is a dusky red infiltrating lesion. There is some itching in the lesions at times. The Wassermann test was negative. The histologic examination showed a picture "compatible with syphilis." Since he has never been treated for syphilis and since there are some clinical features of this disease, I feel that he should be given antisyphilitic treatment as a diagnostic test.

DISCUSSION

DR. H. C. L. LINDSAY: Roentgen rays can be used on some of the lesions for diagnostic purposes. Roentgen rays will usually melt away mycosis fungoides, but their effect on other lesions which simulate mycosis fungoides is relatively slow.

DR. STANLEY CHAMBERS: The clinical characteristics seem to be those of mycosis fungoides. Late cutaneous syphilis of fifteen years' duration should offer more evidence of destruction with repair than is seen here.

Acquired Progressive Kinking of the Scalp Hair with Changes in Its Pigmentation. Presented by Dr. Samuel Ayres Jr.

This case is presented because of its similarity to one reported by M. B. Sulzberger and F. Wise (Arch. Dermat. & Syph. **25**:99 [Jan.] 1932). Both patients were 21 years old. The condition in the reported case was of two years' duration and in this is of four years' duration. No investigation has been carried out, although a determination of basal metabolism and roentgenograms of the skull have been suggested. In the case of Sulzberger and Wise such investigation failed to reveal anything. The authors also made histologic examinations of normal and of abnormal areas of the scalp and expressed the belief that there was no evidence of nevus. In this case the hair was entirely normal four years ago, when this change began. The hair became coarser, shorter, kinked and darker about the front and sides.

DISCUSSION

Dr. C. R. Anderson: I believe the condition is a variant of monilethrix. Under the microscope the hair appeared twisted on its long axis, and there were areas constricted almost to the same degree as in monilethrix.

MINNESOTA DERMATOLOGICAL SOCIETY

Louis A. Brunsting, M.D., *President*

Minneapolis, April 1, 1938

F. W. Lynch, M.D., *Secretary*

Naevus Anaemicus. Presented by Dr. Carl Laymon, Minneapolis.

D. M., a white man aged 24, noted a lesion on the face many years ago. The exact date of onset is unknown. Roentgen therapy in August 1937 proved of no value. The lesion became more noticeable when the face was flushed.

The lesion, which is from 1 to 3 cm. wide in different places, is located on the left side of the forehead and face, starting 1 cm. above the hair line and coursing in a linear manner down the left side of the nose and upper lip. There are no changes in the consistency of the skin, no alterations in the color of the hair and no zone of hyperpigmentation. Histologic sections show pigment in the basal cells of the epidermis.

DISCUSSION

Dr. Carl Laymon, Minneapolis: When I saw this condition, I thought of three possibilities: morphea, vitiligo and naevus anaemicus. There was no hyperpigmented zone such as is often seen in vitiligo and no change in the consistency of the affected skin. The histologic picture favored naevus anaemicus. The patient noticed no change in the lesion after receiving roentgen therapy in Cincinnati. He was treated with 450 roentgens filtered through 3 mm. of aluminum in August 1937.

A Case for Diagnosis (Multiple Draining Periurethral Sinuses). Presented by Dr. S. E. Sweitzer, Minneapolis.

J. C., a Jew, has had numerous operations for fistula in ano and partial anal stricture during the past five years. He was admitted to the hospital on Aug. 23, 1937, because of a persistent draining rectal fistula. This was treated surgically, but subsequently a periurethral abscess and a draining sinus over the left groin developed. After a stormy course and the employment of several surgical procedures to establish drainage, the patient was accepted by the dermatologic service for fever therapy. At the time of transfer he presented a draining sinus over the right groin and over the perineum. He was given six fever treatments, during the course of which the drainage promptly ceased and the sinuses healed.

At present there are several scars showing the locations of the lesions. A Frei test with mouse brain antigen gave a negative result. The Mantoux test with a 1:1,000 dilution gave a 2 plus reaction. Histologic examination showed nonspecific inflammation.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: In cases of urethritis in which no organisms are found the diagnosis of nonspecific urethritis of Galewski is often made. There certainly is a type of urethritis which occasionally causes a periurethral abscess in which no organism can be demonstrated, no matter how careful the examination. Such a condition is a possibility in this case.

DR. F. T. BECKER, Duluth, Minn. (by invitation): This patient was seen about a year ago at the University Hospital, Minneapolis, in consultation by the dermatologic staff. At that time he had a rectal mass producing a stricture. Numerous Wassermann and Frei tests at that time gave negative results. Histologic examination showed anal inflammation. He was given a therapeutic trial of antisyphilitic therapy without any response. He disappeared from observation. Because of the favorable response which he has apparently made to fever therapy at this time, I should suggest a diagnosis of lymphogranuloma venereum in which the Frei test has given repeatedly negative results. Several cases of such a condition have been reported in the literature.

DR. H. A. CUMMING, Minneapolis (by invitation): A report received by me from the University of Minnesota Hospitals on Oct. 12, 1937, stated that the patient was operated on in that hospital for an internal rectal fistula and sinal tracts in July 1933. Again in May 1936 he was admitted to the same hospital, and histologic examination of an indurated nodule in the rectum was made. The sections showed only chronic inflammation. A Frei test with mouse brain antigen gave a negative result at that time, as did a Mantoux test. The Kline and the Kahn test were positive. The Wassermann reaction of the spinal fluid was negative. Although the diagnosis could not be proved, the final opinion of the surgical staff of the University Hospitals was that the patient had lymphogranuloma venereum. I might add that a definite diagnosis of syphilis was never made; however, some antisyphilitic treatment was given as a therapeutic test, in spite of the lack of clinical or serologic evidence of syphilis.

Morphea. Presented by DR. S. E. SWEITZER, Minneapolis.

S. B., a woman aged 48, states that in the middle of July 1937 a generalized eruption "like prickly heat" appeared. The itching was intense, and she suffered from severe headaches. About a week later she noted that the skin over the left side of her neck and the left shoulder was hard and felt "stiff." This condition spread from the left to the right side and somewhat inferiorly along the spinal column. A similar patch soon developed on the left thigh, and several smaller areas on the abdomen. The involved areas were itchy. The size of the areas involved, the itching and the sensations of pressure have steadily progressed. Aside from the necessity for ten months' rest in bed in 1927 because of pulmonary tuberculosis, the patient's health has been excellent.

This patient was admitted to the Minneapolis General Hospital several months ago and was given six hyperpyretic treatments at biweekly intervals, after which her skin was clinically improved. New sections were made and examined.

There is an area on the back over which the surface of the skin appears smooth and has a yellowish white tinge. The skin in this area is tense and hard and cannot be picked up between the thumb and the forefinger. Several small lesions are present on the abdomen and a larger one on the left thigh. The histologic picture was consistent with a diagnosis of scleroderma.

DISCUSSION

DR. L. H. WINER, Minneapolis: Clinically this patient's skin has become much more pliable and soft. Histologically, however, the sections taken after hyperpyretic therapy are identical with those before.

Acrodermatitis Chronica Atrophicans. Presented by DR. H. E. MICHELSON, Minneapolis.

G. V., a man aged 56, first noticed slight scaling on his buttocks and elbows thirty-six years ago. Sometime later his knees and legs became involved. Gradually his skin assumed a pink hue, and the underlying veins became prominent. The only symptoms have been mild itching and easy bruising of the skin. The condition has been extensive for fifteen years.

The skin of the legs, the arms, the back and the lower part of the abdomen is pink, thin and atrophic. It shows marked cigaret paper wrinkling, and the underlying veins are prominent. The elbows show some fibrous thickening, and the forearms and legs are severely involved. There is one area of pseudoscleroderматous thickening 13 or 14 cm. in size on the back.

DISCUSSION

DR. RALPH RAYMOND SULLIVAN, Minneapolis: One is impressed with the wide distribution of countries from which persons with this condition come. The impression seems to have been gained that patients with this disease are always foreign born and like those with Kaposi's sarcoma tend to come from a certain area of Europe. I have reviewed the cases reported in the American literature. Most European countries were represented, and at least a small number of authenticated cases involved American-born persons. Too much emphasis is probably placed on the factor of foreign birth. This man is of further interest because his process began on the thigh rather than over the extremities, and he does not present any tumor formations or sclerotic bands. He shows none of the sclerotic or "hide-bound" skin over the lower part of the leg and the dorsa of the feet. The entire process is much less marked on the hands and feet than anywhere else on the body. It does not stop at the characteristic points, just at the level of the scrotum or groin. Rather, it has gone up the posterior surface almost to the scapula. The outstanding feature of this case, it seems to me, is the extremely marked display of the vascular network through the atrophic skin. This case brings out well the fact that the whole picture is far from being uniform.

Superficial Circumscribed Sarcoid. Presented by DR. S. E. SWEITZER, Minneapolis.

J. P., a white woman aged 65, first noted an eruption on her forearms, arms, neck and face three years ago. She thinks the rash followed the taking of some medicine which was given her for an infection in her ankle. The eruption has remained with no change for the past three years. Her health was good until about three years ago, when she began to grow weak and lose weight. These symptoms progressed until she became bedridden.

There are multiple yellowish brown macules 0.5 cm. in diameter on the extensor surfaces of both forearms and arms, and a few lesions over the neck and face. They are discrete, atrophic and round and show from one to four keratotic plugs near their center. The surrounding skin is normal, and there is no evidence of acute inflammation.

The results of routine examination of the blood, the urine and the spinal fluid were normal. The stools were found to contain no blood, but urobilin and urobilinogen were present (4 plus). The sugar content of the blood was normal, as was the electrocardiogram. A Mantoux test gave a negative result. Roentgen studies of the abdomen and the chest showed no pathologic changes.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I think the time has come when any one presenting a case in which a diagnosis of sarcoid has been made must report observations on other tissues besides the skin. A careful study of the lungs, the bones and the glandular system, as well as the blood, should be made. Only

when this is done can this syndrome be evaluated. Sarcoid is not a cutaneous disease and not a systemic disease but apparently a disease of the entire organism, and the tissues involved, of course, to some degree regulate the signs and the severity. Sarcoid of the skin if left alone progresses slowly, attains a certain size and then regresses, healing with a scar. However, I have seen sarcoid lesions of the skin that evolved rapidly and disappeared rapidly. For this reason I have no confidence in any therapy available at present.

DR. STEPHAN EPSTEIN, Marshfield, Wis. (associate member): I agree with the diagnosis as presented. The impression of frequent internal complications gained from the foreign literature may be misleading. Naturally, more cases of sarcoid with complications are presented or reported than of sarcoid without complications. Among the cases of sarcoid and lupus pernio in which I have made roentgen examination from 1930 to 1935 at the University Skin Clinic, of Breslau, Germany, I remember only 1 or 2 instances of marbling of the lungs, although roentgenograms were taken in all cases.

DR. F. T. BECKER, Duluth, Minn. (by invitation): It is interesting to note that in the American literature the condition described by R. R. Mellon and L. G. Beinhauer (Pathogenesis of Noncaseating Tuberculosis of Skin and Lymph Glands, ARCH. DERMAT. & SYPH. **36**:515 [Sept.] 1937), which resembles Schaumann's benign lymphogranulomatosis, has occurred only in Negroes. Their concept that the causative organism is a transitional form of the Koch bacillus must have further clinical substantiation. Apparently this is an unusual form of noncaseating tuberculosis of the skin occurring in anergic persons.

Tuberculosis (Nodes, Bones and Epididymis); Periarteritis (Tuberculous?). Presented by DR. D. D. TURNACLIFF, Minneapolis.

During the fall of 1934 this patient was presented because of a picture diagnosed as tuberculous glands of the neck, erythema induratum of the right leg and back and an infection of the same origin in the bones of the skull and in the left tibia. The cranial lesion healed after surgical measures, although there was destruction of both tables of the bone. The lesion on the tibia was completely curetted out once, and sequestrums have been removed several times. The origin of this lesion was in the periosteum; the marrow was not involved. In August 1937 several subcutaneous nodular lesions developed on both legs. One on the left thigh was excised; the wound healed, and then, after three months, it broke down and has drained since. Within the past week a swelling of the right epididymis with the characteristics of tuberculosis has developed.

Roentgen studies of the chest in 1934 showed calcifications of an old primary infection. A Mantoux test in 1934 showed a 4 plus reaction and left a scar. The Wassermann reaction was negative. The luetin test gave a negative result.

Dr. E. T. Bell, pathologist at the University of Minnesota, watched the operation on the leg and after examining the material removed reported chronic inflammation. He reported a diagnosis of periarteritis for the excised lesion on the right thigh. The glandular material was lost; so there is no pathologic report on that. The differential blood count was normal. The sedimentation rate was 37 mm. in one hour in November 1937 and 44 mm. in March 1938. The pathologists have observed no specific evidence of tuberculosis at the various biopsies. Certainly this man has had infection in the terminal vessels or some infection producing granulomatous lesions clinically suggesting tuberculosis. Fungous infection and Hodgkin's disease have been suggested as possibilties by Dr. Bell.

DISCUSSION

DR. D. D. TURNACLIFF, Minneapolis: Periarteritis was the only diagnosis Dr. Bell would make on the specimen removed from the thigh. The glands of the neck unfortunately did not get to a pathologist. Since the time of the last biopsy the patient has had a series of lesions of the same origin which did not

produce a histologic picture of tuberculosis. In this case there are lesions in the glands, the bones, the skin and the epididymis, some of which (those of bone and skin) did not show the characteristic histologic picture, while that of the epididymis did. My opinion is that the whole picture is that of tuberculosis.

NOTE.—A biopsy specimen removed from the epididymis after presentation showed the characteristic structure histologically; inoculation of a guinea pig gave a negative result.

A Case for Diagnosis (Onycholysis?). Presented by DR. JOHN BUTLER, Minneapolis.

Urticaria Pigmentosa. Presented by DR. S. E. SWEITZER, Minneapolis.

Urticaria Pigmentosa. Presented by DR. H. E. MICHELSON, Minneapolis.

Postinflammatory Melanosis. Presented by DR. S. E. SWEITZER, Minneapolis.

Pemphigus Vulgaris. Presented by DR. S. E. SWEITZER, Minneapolis.

Extensive Pigmented Nevi. Presented by DR. S. E. SWEITZER, Minneapolis.

Multiple Superficial Epithelioma. Presented by DR. S. E. SWEITZER, Minneapolis.

Swelling of the Heels. Presented by DR. S. E. SWEITZER, Minneapolis.

Lichen Spinulosus. Presented by DR. S. E. SWEITZER, Minneapolis.

Pseudopelade. Presented by DR. S. E. SWEITZER, Minneapolis.

Lichen Planus of the Eyelids. Presented by DR. S. E. SWEITZER, Minneapolis.

A Case for Diagnosis (Mycosis Fungoides?). Presented by DR. H. E. MICHELSON, Minneapolis.

Annular Sarcoid. Presented by DR. S. E. SWEITZER, Minneapolis.

MANHATTAN DERMATOLOGIC SOCIETY

ANDREW J. GILMOUR, M.D., *President*

April 12, 1938

ANTHONY C. CIPOLLARO, M.D., *Secretary*

Eczema Diffusum Resembling Mycosis Fungoides. Presented by DR. FRED WISE.

R. G., a woman aged 55, born in Russia, was first examined at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 2, 1938. She presented a generalized patchy eczema, dry in some areas and exudative in others. The entire eruption showed evidence of much scratching and

rubbing. The duration of the trouble was about one year. She stated that for several months she had been a patient in a ward in one of the local hospitals, where a microscopic diagnosis of mycosis fungoides was made on a lesion excised from the chest.

Of chief interest were lesions on the face, which were elevated, edematous, oval and discoid formations ranging in diameter from 0.5 to 2 cm. and rather soft to the touch. These resembled the infiltrated early lesions of mycosis fungoides. However, after several days of consistent application of a mentholated calamine lotion, these elevated plaques flattened and showed evidence of rapid involution, with considerable abatement of pruritus and burning sensation.

Examination of the widespread eczematous lesions on the trunk and extremities failed to show any manifestations which suggested mycosis fungoides on clinical grounds. Moreover, the eruption on the trunk and the extremities exhibited a prompt response to soothing topical applications.

The object of presentation is mainly to demonstrate an eczematous dermatitis in which a microscopic diagnosis of mycosis fungoides was suggested but not established on the basis of definite histologic observations.

DISCUSSION

DR. ISADORE ROSEN: I had this patient in my service at the Mount Sinai Hospital for several months, and she presented the clinical features seen this evening. Dr. Wise was incorrectly informed by the patient regarding the histologic picture. My histologic diagnosis, made after repeated biopsies, was chronic dermatitis.

This case fits in well with the series recently reported by M. B. Sulzberger and W. Garbe (ARCH. DERMAT. & SYPH. **36**:247 [Aug.] 1937). I described the condition some two years previously (ARCH. DERMAT. & SYPH. **31**:133 [Jan.] 1935; **32**:963 [Dec.] 1935) as belonging to a group of chronic generalized eczema which at various stages shows some of the features first of allergic dermatitis, second of psoriasis, parapsoriasis and lichen planus and finally of mycosis fungoides. I am of the opinion that there is a neurogenic element associated with this group of eczema.

Arsenoresistant Psoriasiform Syphilid. Presented by DR. DAVID BLOOM.

C. C., a married woman aged 36, states that ulceration and swelling of the left labium majus developed four months ago. She consulted a physician, who found a strongly positive Wassermann reaction. Her husband, who had an eruption on the palms and soles, was examined at the same time, and he also showed a strongly positive Wassermann reaction. Both received weekly injections of an arsphenamine preparation. After two intravenous injections the husband's eruption disappeared entirely. This patient's ulcer and the swelling of the vulva disappeared soon, but after two intravenous injections, cutaneous lesions started to appear on the dorsal surface of the hands and fingers and gradually spread to all the extremities and finally to the face, in spite of the administration of twelve intravenous injections. The patient states that she reacted to each injection with nausea, vomiting and chills.

The eruption is situated around the nails, on the backs of the fingers and hands, on the extensor surfaces of the forearms, legs and feet, on the elbows and knees, on the flexor surfaces of the thighs and on the buttocks. It consists of somewhat raised erythematous lesions varying in size from that of a dime to that of a quarter and covered with white scales. The lesions impress one as being more infiltrated and edematous than psoriasis. On the nose and adjacent parts of the cheeks there are superficial plaques of slight erythema and scaling. There is general adenopathy. The Wassermann test with the alcoholic antigen gave a negative reaction and with the cholesterolized antigen an indefinite reaction; the Kahn test gave a negative reaction. After two injections of a bismuth preparation the cutaneous eruption improved, the lesions became much less scaly and lost considerably the appearance of psoriasis.

NOTE.—Several days after presentation a Wassermann test made in another reliable laboratory showed a 4 plus reaction, and several weeks later a Wassermann test done at the first laboratory showed a 1 plus reaction with the alcoholic antigen and a 2 plus reaction with the cholesterolized antigen. The lesions started to lose their scales soon after the beginning of treatment with bismuth subsalicylate and are undergoing gradual involution.

DISCUSSION

DR. HOWARD FOX: I agree with the presenter's diagnosis and also that this disease is sometimes unusually resistant to treatment. There was a case similar to this recently in the Bellevue Hospital; the patient had received one hundred and fifty injections of arsphenamine. I suggest fever therapy followed by the usual chemical therapy.

DR. ISADORE ROSEN: I agree with the remarks of Dr. Fox regarding some cases of psoriasiform syphilid. In my experience these resistant late secondary syphilitic eruptions respond to hyperpyrexia. I think it is a valuable therapeutic procedure.

DR. MIHRAN B. PAROUNAGIAN: I am sorry that I do not agree with the previous opinions. I do not dispute that this woman has syphilis, but I do not think these lesions are syphilitic. She has a symmetric eruption on the extensor surfaces with typical psoriatic scales. The picture is entirely different from that in the case which Dr. Rosen is going to present tonight. There are no circinate or serpiginous lesions, and four months after infection psoriasiform lesions of that type do not appear. I believe that a biopsy is the only thing that will decide the diagnosis.

DR. DAVID BLOOM: When the patient first came to me, the lesions were much more scaly than they are today. However, I favored the diagnosis of psoriasiform syphilid, (1) because of the slightly greater infiltration than is usual in psoriasis, (2) because the scales did not cover the entire lesion but left a small area of the periphery free and (3) because of the lesions around the nails, which I do not remember seeing in psoriasis but which I have seen repeatedly in syphilis. The lesions in the mouth did not suggest mucous patches. Dark field examination carried out once on one of the lesions of the body did not show any spirochetes. This case is of interest because the eruption in the husband responded to treatment while lesions continued to develop in this patient during the same treatment. She received only arsphenamine from her physician, and it is possible that the persistence of these lesions has some connection with this mode of treatment. I shall give her a bismuth preparation, and if this treatment fails, fever therapy will be administered.

Argyria Confined to Bulbar Conjunctivas. Presented by DR. MAURICE COSTELLO.

F. S., a woman aged 28, presents a slate blue discoloration of both bulbar conjunctivas and lacrimal carunculas. She states that fifteen years ago she was advised to instil a drop of mild protein silver in each eye twice a day and continued this for several months. When this condition was first observed several months ago, the patient was unaware of its existence. There is no discoloration of the skin of the eyelids or of the lunulae of the finger nails.

Darier's Disease. Presented by DR. HOWARD FOX.

T. G., a woman aged 27, a dental assistant, has suffered from an eruption of the palms and soles as long as she can remember. During the past six years lesions have been present on the chest and back, and they have become much more noticeable in the past five weeks. She has two sisters and one brother. No member of her family has ever suffered from a similar disease.

The eruption affects chiefly the chest, the supraclavicular and deltoid regions, the upper parts of the breasts, the upper part of the back and the palms and soles.

The eruption is dry and feels like a nutmeg grater on palpation. It consists of reddish pinhead-sized scaly papules which tend to coalesce. She complains of moderate itching, though no marks of scratching are present. The patient is well nourished, mentally active and in apparent good health.

A Case for Diagnosis (Fibroma?). Presented by DR. ANDREW J. GILMOUR.

A. F., a woman aged 74, is an inmate of a state hospital because of arteriosclerotic psychosis.

The patient presents a pendulous tumor with its origin in the left posterior axillary fold. The duration of the tumor is at least five years. There is no history of injury at the site of the lesion, and there are no symptoms, although the size of the mass causes some inconvenience. Operation was refused.

At the neck the diameter of the tumor is about 5 inches (13 cm.); lower down it is 6 inches (15 cm.). It hangs for about 8 inches (20 cm.). The skin is freely movable over the tumor, which is not tender. Palpation reveals hard lobulated masses under the skin. They are not soft enough for lipoma. Malignant tumor and supernumerary breast can be excluded.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: Transillumination of the growth would help here. It would be unusual for this to be a supernumerary breast.

DR. MAURICE COSTELLO: In spite of the fact that this woman has had this tumor for many years, she states that it did not become enlarged during her pregnancies. This would militate against the diagnosis of supernumerary mammary gland.

DR. DAVID BLOOM: Some of the areas of the tumor feel hard, and I think, therefore, that clinically cancer cannot be excluded.

Herpes Gestationis. Presented by DR. MAURICE COSTELLO.

M. M., a married woman aged 35, a multipara, presents a generalized pruritic eruption of two months' duration, consisting of macules, papules and vesicles on an erythematous base, which began in the umbilical region. She is now in the seventh month of pregnancy. She had a similar attack five years ago, which began two months before the birth of the first child. At that time the eruption began around the umbilicus, spread to the rest of the body and was extremely pruritic. It disappeared, and the itching subsided within ten days after the delivery of a girl. The patient has been pregnant four times, the eruption appearing during the first and the present pregnancy.

DISCUSSION

DR. PAUL E. BECHET: In my opinion the disease is not an entity but dermatitis herpetiformis occurring in a pregnant woman, probably due to the toxemia so common in pregnancy. In corroboration of this belief, I have almost always observed that the condition clears up within two or three months after the birth of the child, to recur occasionally at the next pregnancy.

DR. GEORGE M. LEWIS: In a similar case which I observed, a woman had four pregnancies, and in three herpes gestationis developed. She came under my care during the fourth pregnancy. Since she was free of the eruption in one pregnancy before the birth of a girl, and in both instances when she had attacks of the disease a boy was born, I was interested in the outcome of the fourth pregnancy. As expected, a boy was born. On each occasion the eruption began about the fifth month of pregnancy and disappeared promptly during the puerperium.

DR. E. WILLIAM ABRAMOWITZ: I think these gestational eruptions vary a great deal, but I do not think they all should be classed in the same group as dermatitis herpetiformis. There are some cases in which the eruption takes on the charac-

teristics of erythema multiforme bullosum and the pregnancy has to be interrupted because the systemic symptoms are serious. Most of the eruptions appear in the latter part of pregnancy, and there may be some connection with a female sex principle.

DR. MAURICE COSTELLO: In many cases reported in the literature herpes gestationis occurred only in the pregnancies terminating in the birth of infants of the same sex. This particular patient's first child was a girl. It will be interesting to see if the present pregnancy terminates with the birth of a girl.

Nonpigmented Melanoma. Presented by DR. GEORGE C. ANDREWS.

S. C., a man aged 40, has a lesion on the chin of two years' duration. It began after a cut from shaving, appearing first as a swelling, which was burned off by a local physician. Another nodule formed and was also burned off, but it recurred and gradually grew to the present size.

Examination shows a nodular yellowish white lesion 1.7 cm. in diameter on the left side of the chin. There is marked induration beneath the lesion, which is stony hard when palpated. There are no palpable glands in the submental or the cervical region. A microscopic examination showed the structure of extremely atypical naevus pigmentosus. Beneath an atrophic epidermis in the corium there were nests of large polygonal cells with huge nuclei. Many of the nuclei were undergoing mitosis. No melanin was demonstrated; multinucleated cells were present. Trabeculae of connective tissue gave the tumor a lobulated structure. Foci of lymphocytic infiltration were present. The histologic diagnosis was nonpigmented melanoma.

The patient has received two courses of eight daily treatments of roentgen radiation by a modified Coutard technic (160 kilovolts, filtered through 0.5 mm. of copper and 1 mm. of aluminum, for a total of 2,400 r).

At present there are epilation and intense erythema of the treated area, but the lesion has flattened to the level of the skin, although induration is still palpable. Another course of roentgen treatment is contemplated for next week.

DISCUSSION

DR. J. FRANK FRASER: This tumor is malignant. Such growths are usually radioresistant.

DR. ISADORE ROSEN: I should like to ask the presenter whether he had roentgenograms made of the chest. It might be well to investigate the possibility of metastases in the chest.

DR. GEORGE M. LEWIS: Contrary to general opinion, melanoma responds at times to intensive roentgen therapy. This case reminds me of one of melanoma which Dr. John Remer had ten years ago. When observed recently the patient showed no sign of recurrence and was in vigorous health.

DR. GEORGE C. ANDREWS: I think this patient has responded fairly well. Large doses were employed. I have seen most unsatisfactory results in the treatment of melanoma by radical surgical procedures. Therefore I felt that in this case, in which there was such a large lesion on the chin, one would not be warranted in performing an extremely radical operation, which no doubt would be done if the cure was attempted by surgical means. That is the reason I resorted to this modified Coutard technic with high voltage roentgen radiation. One can see that improvement has occurred since the latter treatment.

Parapsoriasis with Beginning Mycosis Fungoides. Presented by DR. ANTHONY C. CIPOLLARO.

F. B., a man aged 47, born in the United States of Jewish parents, is presented from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. He states that he has had the present condition for twenty-six years.

The eruption has been persistent since its onset and has cleared only after exposure to sunshine. During the winter he has been able to keep the condition under control with ultraviolet irradiation to the entire body. The condition has never been pruritic.

In March 1937 some of the lesions started to become exudative. Since then he has had several coin-sized patches in different portions of the body, especially on the buttocks and on the legs. These patches have been infiltrated, and some of them have ulcerated. One, two or three fractional doses of unfiltered roentgen rays (75 r) have caused the ulcerated and infiltrated lesions to disappear.

The patient has a generalized eruption, most pronounced on the extremities and the trunk. It consists of erythematous and scaly patches varying in size from that of a split pea to that of a palm and larger. The lesions are discrete for the most part. There are varying degrees of infiltration. The color also varies. The newer lesions are brighter red than the older ones. In some of the plaques on the legs and buttocks there are small infiltrated areas covered by recently formed crusts and scales. A superficial ulcer is present in one small lesion on the right leg.

The blood count was essentially normal. Urinalysis showed no abnormality. Histologic examination of one of the infiltrated plaques showed only dermatitis.

DISCUSSION

DR. PAUL E. BECHET: Although there is no apparent itching, the patient has as typical mycosis fungoides as one could see. There are sharply outlined geographic plaques, some of them infiltrated and some showing degenerated changes. I should not consider the diagnosis of parapsoriasis.

DR. HOWARD FOX: This case presents three features which favor the diagnosis of mycosis fungoides rather than that of parapsoriasis. The patient states that the lesions clear for six months or so during the summer. They are radiosensitive and show varying degrees of infiltration.

DR. ISADORE ROSEN: Some twenty years ago Dr. Fred Wise and I (*J. Cutan. Dis.* **34**:95, 1916) reported 2 cases, 1 of parapsoriasis en plaques and the other of mycosis fungoides. Clinically the two conditions were indistinguishable. However, under the microscope one presented the picture of parapsoriasis and the other that of mycosis fungoides. I still maintain that there are cases in which parapsoriasis remains such and never develops into mycosis fungoides.

DR. J. FRANK FRASER: I think all the members will recall the case that I presented before this society about three years ago (ARCH. DERMAT. & SYPH. **32**:324 [Aug.] 1935). The patient had a generalized scaly eruption, and the majority of the members called it psoriasis. The histologic picture of one of the lesions harmonized with that clinical diagnosis. Within two months tumors with a characteristic histologic picture of mycosis fungoides developed. A review of the slides showing psoriasis showed a nest of reticular cells in one of them, with mitosis—in other words, a histologic picture of mycosis fungoides.

DR. ANTHONY C. CIPOLLARO: This patient has been under my observation for one and a half years. I have considered the lesions to be parapsoriasis of the plaque type. When tumors and ulcerations began to develop, I considered the case one of parapsoriasis of the plaque type changing into mycosis fungoides. Even though the histologic picture was not that of mycosis fungoides, the clinical appearance fits in with this diagnosis. Up to the time the patient placed himself under my care, he had been treated for about twenty-five years by Dr. I. R. Pels, of Baltimore, who considered the case to be one of parapsoriasis of the plaque type.

Resistant Secondary Syphilis. Presented by DR. ISADORE ROSEN.

C. McG., a married woman aged 33, was admitted to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on May 27, 1937, at which time she presented mucous patches on the tongue and the inner

side of the upper lip. On the right labium majus there is an erythematous slightly infiltrated plaque which may be a healing primary lesion. The Wassermann reaction was 4 plus. She received two injections of a bismuth preparation at weekly intervals, after which she allowed treatment to lapse for one month. On her return she received three more injections of a bismuth preparation. On July 31, 1937, an extensive psoriasiform eruption suddenly appeared on the trunk and extremities, particularly over the so-called seborrheic areas. There were scattered coin-sized lesions as well as extensive areas. The essential lesion consisted of a papule, shiny and brownish; many of the lesions showed marked scaling of the type of psoriasis. There were numerous corymbiform lesions. Two dark field examinations on different dates failed to show Spirochaeta pallida.

On Oct. 30, 1937, histologic examination showed papular fichenoid syphilid. Since admission the patient has received twenty-two injections of arsphenamine, four of neoarsphenamine, six of mercury and twenty-three of a bismuth preparation.

At first the lesions responded to treatment; many have cleared up entirely, leaving pigmented areas. However, new lesions are appearing constantly, chiefly on the trunk and the extremities. These are serpiginous with clear centers.

A Case for Diagnosis (Tuberculid?). Presented by DR. FRED WISE.

B. F., a single American woman aged 32, was previously presented at the October 1937 meeting of the New York Dermatological Society (ARCH. DERMAT. & SYPH. **37**:896 [May] 1938).

Since the previous presentation the patient has undergone another complete examination during a two week stay at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. This included complete study of the blood roentgen examinations and microscopic studies of one of the purpuric lesions on her arm. The histologic report stated that the section showed merely an urticarial type of lesion. Tuberculin and Wassermann tests gave negative results.

The patient is again presented, to obtain further suggestions as to diagnosis and treatment.

DISCUSSION

DR. GEORGE C. ANDREWS: I have been thinking about this case, and I believe that it is one of dermatitis nodularis necrotica described by Werther (I Konegraphia, 1910, p. 213) and by W. W. Duemling (ARCH. DERMAT. & SYPH. **21**:229 [Feb.] 1930). They reported hemorrhagic lesions, some of which occurred in the mouth. I had a similar case in which there were no lesions in the mouth but some were present on the trunk. Most of Duemling's patients eventually died, but some of them were helped by treatment.

Dermatophytosis (Immediate Wheal Reaction to Trichophytin). Presented by DR. GEORGE M. LEWIS.

S. S., a domestic servant aged 18, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, had recurrent attacks of an inflammatory eruption on the fingers during the past two years. For three months there were acute vesicobullous lesions on the soles and the palms, interdigital maceration of the feet and dystrophic changes in two finger nails. The condition when observed was subsiding. Fungi were demonstrated in material from both the hands and the feet. Cultures have not yet grown. Trichophytin tests showed marked wheal reactions within ten minutes and negative reactions after forty-eight hours. Repetition of the test with a minute quantity of well diluted trichophytin produced the same immediate response with pseudopods. Trichophytin diluted with the patient's own serum caused as large a reaction as the undiluted trichophytin. Serum and saline solution in the same concentration used as a control gave a negative reaction.

DISCUSSION

DR. GEORGE M. LEWIS: It has been my observation that patients with primarily inflammatory tinea invariably show a positive reaction to the trichophytin test. Some patients, as in this case, exhibit an immediate wheal reaction. For that reason the reaction should always be read after fifteen minutes.

Angiosarcoma of the Hand and Arm. Presented by DR. FRED WISE.

M. C., a woman aged 24, was first examined at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, March 17, 1938. Three years ago she first noticed a dime-sized lesion on the back of the left hand, at the base of the index finger. This resembled an elevated brown mole, which was painless and not tender. The lesion was excised, and microscopic examination showed it to be angiosarcoma. Shortly after excision of the primary lesion, a hickory nut–sized mass appeared on the inner surface of the left forearm; this was adherent to the underlying tissue, and the skin over it remained unchanged.

Examination shows a small scar at the site of the excised lesion and a globular firm subcutaneous tumor on the inner aspect of the left forearm, 4 inches (10 cm.) above the wrist. Another tumor of similar consistency but spindle shaped and about 2 inches (5 cm.) long, is palpable just above the elbow in the cubital area. There is no axillary involvement. The patient states that there are no subjective symptoms. Roentgenograms of the chest showed no abnormalities.

Linear Eruption Resembling Lichen Planus in a Syphilitic Patient with an Arsenical Dermatitis. Presented by DR. PAUL E. BECHET.

A. D., a young Negress, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, states that she had a syphilitic infection with positive serologic findings. After the administration of eight intravenous injections of an unknown quantity of arsphenamine, an eczematoid vesiculopapular eruption developed on the upper part of the trunk, the neck and the face. Several weeks later she noticed a linear, papular eruption, beginning at the crural fold and extending in a single line down to the foot. Both eruptions had persisted for some two months at the time of her first visit to the clinic. Careful examination of her body failed to show any corroboration of the rather typical linear lichen planus on her leg. The eczematoid dermatitis on her neck was still evident. The arsenical content of the blood was 0.04 mg. per hundred cubic centimeters.

DISCUSSION

DR. DAVID BLOOM: I have observed a few cases of linear eruption along one upper extremity in which the diagnoses of lichen planus and linear dermatitis were considered clinically and in which the microscopic examination decided the diagnosis in favor of dermatitis. Therefore, I believe that in this case the linear eruption along the lower extremity is dermatitis and is a part of the generalized arsphenamine dermatitis.

DR. E. WILLIAM ABRAMOWITZ: I believe this eruption is linear lichen planus following administration of arsphenamine. However, I have seen sections taken from similar lesions showing characteristics of linear nevus, lichen planus, psoriasis or even syphilis.

Leukaemia Cutis. Presented by DR. HOWARD FOX.

S. G., a man aged 54, a teacher, is presented from the dermatologic wards of the Bellevue Hospital. About one year ago he began to complain of generalized pruritus, and within a few months a generalized eruption developed. On admission, on Feb. 7, 1938, he presented a universal scaling erythroderma with numerous papules, crusts and excoriations. There was moderate generalized lymphadenopathy.

The spleen could not be palpated. A roentgenogram of the chest showed no lymphatic enlargement.

Examination of the blood on March 10, 1938, showed 34,250 leukocytes, with a differential count of 8 per cent metamyelocytes (no. 2), 29 per cent polymorphonuclear leukocytes, 33 per cent lymphocytes, 1 per cent monoblasts, 2 per cent promonocytes, 6 per cent monocytes and 21 per cent eosinophils. (Some of the lymphocytes showed segmentation of nuclei.) There were 4,810,000 erythrocytes and 93.1 per cent (13.6 Gm.) hemoglobin. The color index was 0.9. The mean corpuscular volume was 83 cubic microns and the mean corpuscular hemoglobin 28 micromicrograms (concentration 34 per cent); a test for fragility of erythrocytes showed beginning hemolysis in 0.46 per cent and complete hemolysis in 0.32 per cent saline solution (control 0.46 and 0.36 per cent); clot formation was normal and clot retraction good.

Histologic examination of a lymph node by Dr. Douglas Symmers showed giant follicular lymphadenopathy. Histologic examination of skin from the arm showed leukemic infiltration.

High voltage roentgen therapy was administered to the trunk on five occasions from March 22 to April 8, 1938. During this period the leukocyte count fell from 37,680 to 10,200 and there was a decided improvement in the eruption.

Chancroidal Ulcer of Long Duration Cured with Sulfanilamide. Presented by Dr. Howard Fox.

J. J., a Negro aged 40, presented from the dermatologic wards of the Bellevue Hospital, suffered previously from an ulcer involving the greater part of the glans penis. Both autoinoculation and the Ito-Reenstierna tests gave positive results. The Frei test gave a negative result. He was given sulfanilamide in doses of 5 Gm. for five days, followed by daily doses of 3 Gm. for twenty-eight days. At the end of this period the ulceration had entirely healed. He now presents deforming scar tissue of the distal two thirds of the glans penis. The urethra empties freely through the center of the scar. Leukocyte counts at the beginning and toward the end of treatment showed approximately 12,000 white blood cells. The differential count on each occasion was normal.

A Case for Diagnosis (Phagedenic Chancroid?). Presented by Dr. Howard Fox.

R. H., a Negro aged 39, is presented from the dermatologic wards of the Bellevue Hospital. For the past year he has suffered from an ulceration which involves the prepuce and the proximal third of the glans penis. There are slight phimosis and moderate elephantiasic enlargement of the entire penis. There is no inguinal adenopathy. The Wassermann and the Frei test and smears for gonococci gave negative results. The Ito-Reenstierna test gave a positive result, but the autoinoculation test gave a negative result.

Note.—A biopsy was performed subsequent to presentation, and the microscopic examination showed simple inflammatory tissue. Donovan bodies were not observed. The patient was given a total of 52 Gm. of sulfanilamide, without benefit.

DISCUSSION

Dr. Maurice Costello: Some investigators believe that this medicament is five times as effective when given by intravenous or intramuscular injection as when given by oral administration.

Dr. David Bloom: As far as I know from the literature, there is no difference in the effect of sulfanilamide given intramuscularly or by mouth. Oral administration is at least as good as parenteral injection. The effect of this drug is dependent on an adequate concentration in the blood, and therefore large initial doses should be given, followed by smaller doses sufficient to maintain a satisfactory level of the drug in the blood over a considerable length of time.

Discoid Lupus Erythematosus Undergoing Dissemination. Presented by Dr. Fred Wise.

W. G., a man aged 51, born in the United States, was first examined on May 15, 1937, at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. In the past twelve years he has had an eruption of lupus erythematosus on the cheeks, ears and neck. There have been partial remissions at times but no decrease in the extent of the eruption. The affected areas are dark, red and thickened in some places and atrophic in others; they form a more or less diffuse and widespread eruption involving almost the entire face and spreading from there to the ears and neck. A year ago reddish blue macular spots made their appearance on the backs of the hands. These are now well defined somewhat scaly violaceous patches, chiefly on the backs of the fingers. The patient's general health was said to be fairly good, but on presentation his temperature was 100.4 F., and he complained of feeling "run down."

He received twenty injections each of sodium gold thiosulfate solution and an insoluble bismuth preparation without noticeable improvement of the eruption. He is presented for suggestions concerning the advisability of administering sulfanilamide.

DISCUSSION

Dr. E. William Abramowitz: I have had some experience with oral administration of sulfanilamide, and I think there is no difference in effect—in fact, I think the drug works better when given by mouth than by injection. I have never observed recovery in a case of acute disseminate lupus erythematosus during the many years that I have been practicing. For the first time, since I have used sulfanilamide, I have been able to send 3 patients out of the hospital considerably improved. I gave the standard doses. One interesting case was that of a young woman who had her spleen removed for thrombopenic purpura. She had a low blood platelet count and leukopenia, associated with acute disseminated lupus erythematosus. She was given sulfanilamide, but the medication had to be stopped after a few days and quinine given, as the platelet count dropped dangerously low. She improved considerably, although new lesions appeared from time to time. At present she is practically well. If a patient with chronic discoid lupus erythematosus does not respond to the usual conventional remedies (gold and bismuth preparations) sulfanilamide may be given a trial.

Dr. David Bloom: I have tried sulfanilamide in 5 or 6 cases of lupus erythematosus at the Bellevue Hospital. In some initial improvement followed one or two injections, but this improvement did not continue. In 1 patient high fever developed after injection of a derivative of sulfanilamide known as prontosil (the disodium salt of 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonic acid), and I have since then administered sulfanilamide per os. One of the patients could stand only one tablet of 5 grains a day. When this dose was increased she reacted with generalized erythema and discomfort. A persistent lesion on the chest and one on the nose disappeared within a short time. Severe pruritus of the face developed in another patient after daily ingestion of 15 grains (0.97 Gm.) for one week. This necessitated the discontinuation of treatment. In the other cases there was no effect at all following daily ingestion of 15 grains (0.97 Gm.) of sulfanilamide. I did not dare to administer larger doses in my cases of lupus erythematosus.

A Case for Diagnosis (Tinea Barbae?). Presented by Dr. E. William Abramowitz.

B. K., a man aged 34, driver of a horse-drawn laundry cart, came to the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on April 11, 1938, with an eruption on the sides of the neck, the eyebrows, the nose and the lips of seven weeks' duration.

The first eruption appeared on the left side of the neck as a dime-sized furuncle-like lesion that spread out centrifugally until it occupied a palm-sized area with a clear center and an elevated border made up of many pustular lesions. During the following three weeks a similar development took place on the right side of the neck. The patches spread over the angle of the jaw. Small red crusted lesions developed on the lips, with a solitary patch on the back of each hand and a dry, dime-sized erythematous patch on the glans penis. Erythema with ill defined borders was present on the bridge of the nose and the eyebrows.

He had been under the care of a physician who gave him about six injections of bismuth subsalicylate, but the eruption continued to spread. Several Wassermann and Kahn tests had been made and were reported negative. Repeated questioning elicited no history of medication.

Numerous smears and cultures for fungi were negative. Examination of the urine showed no abnormality.

NOTE.—A microscopic examination made later showed mostly polymorphonuclear infiltration around the vessels of the cutis with subepidermic vesicles. The picture might conform with deep tinea. A blood count and examination of the urine for bromides and iodides were ordered.

DISCUSSION

DR. PAUL E. BECHET: I think the condition in this case belongs to that rather interesting group of dermatoses described as lupus erythematosus of the moist or the acute vesicular type.

DR. MIHRAN B. PAROUNAGIAN: On account of the duration and the raised elevated borders, I am inclined to agree with the diagnosis of tinea as presented.

Erysipeloid of Rosenbach. Presented by DR. GEORGE M. LEWIS.

C. C., a locksmith aged 49, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, has had lesions on the backs of his fingers on and off for two years. The lesions have been present constantly for the past six months. He handled clams just prior to the onset. There are no subjective symptoms. The lesions are bluish red slightly elevated plaques and are present on the backs of the fingers. No scaling is present. The palms are not involved. No focus of fungi was found on the feet.

The histologic appearance suggested chronic eczema. There were edema throughout the cutis and an elongation of the rete pegs. The vessels were moderately dilated, with thickened walls, and around them there was a sparse simple infiltrate. The epidermis showed marked regular acanthosis with areas of parakeratosis.

A biopsy specimen was planted aseptically in dextrose broth. The resultant colonies consisted of cocci and rods of varying sizes and types and some actinomycetic forms. Agglutination studies gave slightly positive results in a dilution of 1:20 and more positive results in a dilution of 1:2. Controls gave negative results. Injection of 0.1 cc. of a twenty-four hour broth culture of predominantly actinomycetic forms into a mouse produced its death in four days; lesions were present in the liver and the spleen. Cultures have not yet grown.

DISCUSSION

DR. E. WILLIAM ABRAMOWITZ: This case is not one of classic erysipeloid of Rosenbach, because the eruption is bilateral, with no history of advancing from one area to another.

DR. ANDREW J. GILMOUR: My idea of erysipeloid of Rosenbach is that it is not so regularly confined to all four fingers of both hands. I do not believe that in most cases it lasts as long or is as chronic as in this one. I observed a good many cases at the Roosevelt Hospital. In all it was more acute than in this.

DR. GEORGE M. LEWIS: I cannot yet definitely state that the causative organism has been isolated.

Severe Ichthyosis in a Negro. Presented by DR. PAUL E. BECHET.

R. J., a dark full-blooded Negro aged 14, from the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, presents greatly thickened elevated black hyperkeratotic patches covering most of the trunk. On the legs the scales are laminated and present the usual typical "crocodile skin," or sauriderma. No familial history could be elicited. The disease has been present since birth. The patient is presented because of the extraordinary thickness and deep black color of the patches on the trunk and because of his race.

A Case for Diagnosis (Buccal and Labial Lupus Erythematosus? Pemphigus?). Presented by DR. FRED WISE.

I. W., a man aged 46, born in Austria, was first examined at the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital on June 27, 1937. For the past two and a half years he has suffered from a recurrent eruption on the lips and the buccal mucosa, characterized by severe excoriations which were said to have been preceded by vesicles and small bullae. He complains of pain on eating and difficulty in mastication.

Examination shows an adherent serosanguineous crusted eruption on both lips, most pronounced on the lower. The buccal mucosa is uniformly inflamed and eroded, and the posterior triangles opposite the molar teeth present a reticulated appearance, as seen in lichen planus and occasionally in lupus erythematosus. There is no evidence of vesicle formation. The patient's history excluded ingestion of drugs. The condition improved considerably under graded injections of solution of sodium arsenate. Numerous laboratory investigations, including smears of material from active lesions and studies of the blood, failed to offer a clue to the cause of the erosions. The patient's general health has been consistently good. At no time has there been any eruption on the skin.

DISCUSSION

DR. ISADORE ROSEN: Dr. Wise suggested two diagnoses in this case, pemphigus and lupus erythematosus. I agree with the latter diagnosis. I was unable to find any bullous lesions on the buccal mucosa or the lips. On the inner surfaces of the cheeks are superficial erosions, and the lesions on the lips show slight infiltration and scaling, with a deep violaceous hue. As the patient has had this condition for a year or more without any other evidence of pemphigus, I think it is lupus erythematosus involving only the mucous membranes.

Achromia Parasitica. Presented by DR. LUDWIG OULMANN.

Lupus Erythematosus Disseminatus with Extension After Ultraviolet Irradiation. Presented by DR. PAUL E. BECHET.

Radiodermatitis (in a Patient Treated by a General Radiologist). Presented by DR. DAVID BLOOM.

Lupus Vulgaris. Presented by DR. HOWARD FOX.

Atopic Eczema. Presented by DR. GEORGE M. LEWIS.

BRONX DERMATOLOGICAL SOCIETY

THEODORE ROSENTHAL, M.D., *President*

April 28, 1938

HENRY SILVER, M.D., *Secretary*

Pustular Bacterid (Andrews). Presented by DR. PAUL GROSS.

E. J. C., a truck driver aged 40, was seen at the Hospital for Joint Diseases and at the Vanderbilt Clinic. The eruption began two years ago as small blisters on the left palm; one year later the right hand became affected. About three months ago an eruption appeared on the backs of the hands, feet, elbows, chest and scalp. Several years previously there had been an eruption on the feet, which cleared up entirely. In 1918 the patient was operated on for nasal polyps; in 1919 he had an infection of an ear. He is not in the habit of taking medicine, except an occasional "headache powder."

On the palms there are diffuse redness and slight scaliness. The erythematous area is studded with numerous vesicles and pustules. On the dorsa of the hands, the flexor surfaces of the wrists and the elbows there are vesicles the size of a pea and superficial crusts. On the chest and abdomen are a few irregularly shaped reddish patches with sharp outlines, with slight scaling in the center and a few vesicles on the border. On the dorsa of the feet are erythematous lichenified areas with scattered vesicles. There are scaling and maceration between the toes; several toe nails are thickened and yellowish gray. On the scalp reddish scaly, slightly crusted lesions appear at times. During a recent attack of tonsillitis the eruption flared up considerably.

Scrapings and cultures of material from lesions in various locations showed no fungi or cocci. Examination of the throat revealed chronic tonsillitis; cultures of material from the left tonsil showed hemolytic streptococci. The blood count revealed no abnormalities. Roentgenograms of the teeth showed no infection.

Intradermal tests gave the following results: With staphylococcus toxin the immediate wheal reaction was 1 cm. wide with pseudopods and was surrounded by an area of erythema 2 cm. in diameter; the delayed reaction was a 1 cm. infiltrated papule and an area of erythema 6 cm. in diameter. Streptococcus toxin and monilia extract gave negative reactions. Trichophytin gave a delayed reaction consisting of 1 cm. of erythema with a small vesicle.

Pustular Psoriasis. Presented by DR. DAVID BLOOM.

G. L., a woman aged 39, has had an eruption on the left foot for the past eight years. A similar eruption on the right foot cleared under treatment with ointments. On the heel and on the outer side of the left sole there are a few round denuded patches studded with flat pustules the size of a pinhead. This eruption, which is associated with burning and itching, has resisted all treatment and has never disappeared since its inception. The patient has one living child. She had two stillbirths, attributed by her physician to marked anemia. Tonsillectomy was performed in childhood.

Roentgenograms of the lungs revealed no abnormality. The blood count showed 3,600,000 erythrocytes, 7,500 leukocytes and 63 per cent hemoglobin.

DISCUSSION OF CASE OF PUSTULAR BACTERID AND CASE OF PUSTULAR PSORIASIS

DR. GEORGE C. ANDREWS (by invitation): Dr. Gross's case is the first I have observed in which lesions characteristic of pustular bacterid on the palms and soles are associated with pustular lesions on the elbows, the scalp, the upper parts of the arms and the trunk. The patient has had this eruption for over two years,

and I feel that the question of whether it is pustular psoriasis is of secondary importance. He has never had any lesions of psoriasis and has nothing at the present time that looks like psoriasis. Careful cultures and examinations failed to show fungi in the toe nails, on the feet or on any other part of the body. The trichophytin test gave a slightly positive result, but the reaction to staphylococcus toxin in 1 : 200 dilution, which, by the way, has been in use for a number of years at the Vanderbilt Clinic, was extreme. There was intense erythema over 6 cm. in diameter the day after the test, and this was followed by the development of a deep erythematous nodule. This is unusual. In addition, this patient has chronic tonsillitis and infected teeth. The striking feature in this case is the widespread distribution, which might at first glance suggest Duhring's disease; but lack of the characteristic grouping and the profuse involvement of the palms and soles promptly rule out that diagnosis. The histologic picture is being studied, but tentatively I feel that the condition is generalized pustular bacterid. Of course that term has been questioned repeatedly, especially by the advocates of a diagnosis of pustular psoriasis. In the last few years Dr. H. W. Barber, of London, England, has recognized pustular bacterid as an entity and distinguished it from pustular psoriasis. That there is such a thing as pustular bacterid I do know. It is a definite disease in which a focus of infection, like the teeth or the tonsils, plays a part. In many cases long-standing eruption has been permanently cured by simple removal of the focus of infection. From reports from other parts of the country and from my own practice I know of at least 25 cases in which cure was accomplished in that way. I see no reason to make a diagnosis of pustular psoriasis in this case. Psoriasis is a clinical entity, and the elementary lesions are red flat papules with micaceous scaling and have a definite clinical appearance and course. All these are absent in this case.

Dr. Charles Lerner: I not only agree with everything Dr. Andrews said but should like to go a step further and say that in my opinion pustular psoriasis has a definite relation to bacterial infection. Certainly one encounters cases in which psoriasis clears after the removal of diseased tonsils or the healing of pyorrhea.

Dr. Marion B. Sulzberger: A case of this kind really merits many months' study. Undoubtedly foci of infection have a real influence in some cases of many different dermatoses. Such foci may act as sole causes in a few cases, but in many instances only as contributory factors. It is well recognized that organisms originating in distant foci can produce pustular and eczematoid eruptions, and the older dermatologists—for example, J. Jadassohn, Darier and Bloch—called lesions of this type "microbids" and talked of "staphylococcids" and "streptococcids." Moreover, there is nothing new about the belief and impression that foci of infection may cause cutaneous lesions of other types. Another problem, which is much more difficult to solve, is that of proving by what mechanism foci of infection contribute to the origin of cutaneous lesions. All the members recognize that characteristic psoriasis, dermatitis herpetiformis and lichen planus, as well as many other dermatoses, occasionally clear up after the removal of a focus of infection, but this means not necessarily that the cutaneous manifestations were actually due to the focus, but simply that the focus was acting in a contributory, a synergetic or a predisposing manner. Dr. Andrews has recently given these problems intensive study, and I have discussed this matter with him and others for years. It seems to me that as yet dermatologists are up against a stone wall, so far as elucidating actual mechanisms is concerned. In those of my cases in which removal of foci was of distinct benefit I was nevertheless unable to prove that the focus was the sole cause of the eruption. I believe that in this particular case the lesion on the toe nail is fairly characteristic of psoriasis and that this suggests that the diagnosis of pustular psoriasis merits further consideration.

Dr. David Bloom: If the eruption in Dr. Gross's case were confined only to the palms and soles, pustular psoriasis would be a correct diagnosis. The associa-

tion of papules, vesicles and bullae on the dorsa of the feet and the elbows is in my experience an unusual occurrence. Nevertheless, a provisional diagnosis of pustular psoriasis should be entertained, particularly as there are changes in the toe nails which speak strongly in favor of psoriasis. A definite diagnosis can be made only by long observation, for even if typical psoriasis does not subsequently develop on other parts of the body, the lesions on the palms and soles may assume in the course of time the appearance of typical squamous psoriasis.

In my case a definite diagnosis of pustular psoriasis is justified. The plaques are sharply defined and of many years' duration and have never disappeared entirely, in spite of various methods of treatment. Examinations for fungi have persistently given negative results. The tonsils were removed in childhood, and other possible foci of infection have not been detected.

DR. PAUL GROSS: I agree with everything that Dr. Andrews stated but do not share Dr. Lerner's optimism that typical psoriasis can be cured by removal of foci of infection. Such cure, on the other hand, is an established fact in some of the cases of vesicular, pustular bacterid described by Andrews.

For at least four years I had under my observation a patient with an extensive eruption on the palms and soles, which did not clear up after tonsillectomy but did disappear after removal of a chronically infected appendix (not removed on account of the eruption). On the other hand, pustular psoriasis does exist, and I had the privilege of observing a case of striking involvement when I was in Prof. Karl Kreibich's clinic. The patient, a young girl, was hospitalized several times, and one could follow the lesions from the pustular stage through the dry stage and finally to the formation of a guttate psoriatic lesion. The condition was generalized, without involvement of the palms and soles. In the case presented tonight there is another important feature, seen occasionally in pustular bacterid, namely, the appearance of groups of acute vesicles, which disappear without leaving any psoriasiform lesions.

A Case for Diagnosis (Acanthosis Nigricans? Papillomatose Réticulée [Gougerot]?). Presented by DR. MARION B. SULZBERGER.

S. M., a woman aged 24, a clerk, a patient of Dr. Hans Field, was admitted to the Montefiori Hospital for Chronic Diseases on Jan. 25, 1938. In 1934 she was treated at the Vanderbilt Clinic for ringworm. At that time an eruption appeared on the arms and thighs. From August 1935 to June 1936 she was a patient at the Good Samaritan Dispensary and Hospital (Essex St., New York), where a diagnosis of neurodermatitis was made. In July 1936 she was seen at the Mount Sinai Hospital, where a diagnosis of atopic dermatitis was made. From October till December 1937 she was visiting the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital. Microscopic examination of a section from the dorsal aspect of the right wrist showed changes suggestive of psoriasis.

The clinical picture at the beginning was that of diffuse neurodermatitis with marked scratch effects and lichenification predominantly over the chest, abdomen, buttocks, back and neck and less marked on the arms, legs and face. The backs of the hands and the dorsal aspects of the forearms showed intensive lichenification and thickening of a papillomatous type. Physical examination showed no essential abnormality. As yet no sign of malignant growth in the abdomen has been found, and the patient is gaining weight. There is generalized enlargement of the accessible lymph nodes.

At present the interesting features are the marked papillomatous changes which appear as bright flesh-colored and almost velvet-like dry elevations, separated by superficial and deeper furrows. On the whole they give the impression of an exaggeration of the normal cutaneous markings. The most involved area is the neck, which shows diffuse papillomatosis arranged like a collar and extending to the ears and the posterior parts of the neck. Similar but less pronounced lesions

are seen on the axillas, the inguinal folds, the midline of the chest, the submamillary folds, the nasolabial folds and the flexor surfaces of the knees. Analogous lesions are scattered over the scalp. The sites of predilection are those of acanthosis nigricans. The patient believes that she noticed these peculiar changes two years ago. These processes have recently increased in intensity.

Studies of the blood, including chemical analysis, urinalysis and serologic tests showed no abnormality, with the exception of a high degree of eosinophilia. Owing to the present superimposed impetiginous lesions, particularly on the scalp, further investigations have been postponed.

DISCUSSION

DR. WILBERT SACHS: I saw this patient three or four years ago. At that time she presented a generalized eruption which followed dermatomycosis of the feet; it then suggested either lichen acuminatus or an "id." The microscopic report "suggestive of psoriasis" should be disregarded.

DR. ARTHUR SAYER: I believe that in time pigmentation will gradually develop in the papillomatous regions. Further observations of this patient will prove the case to be one of acanthosis nigricans. I suspect this outcome because I have a similar case under my observation. In a patient whom I treated for psoriasis pigmentation and velvety lesions developed around the neck and in the groins. There was associated gastrointestinal disturbance. Malignant tumor of the intestines subsequently developed.

DR. ERICH URBACH, Vienna, Austria (by invitation): I had occasion to see this patient a few days ago with Dr. Sulzberger and recognized the peculiar and unusual character of the eruption. There are various types of lesions, but the most interesting are those that are hyperkeratotic. I cannot make a definite diagnosis but should like to point out the resemblance to a disease which I described as lipoidosis cutis. In my entire experience I have never encountered a case in which the hyperkeratosis so closely resembled lipoidosis cutis. I therefore suggest investigation along this line. It may be that this dermatosis is a new kind that has not been seen before.

A Case for Diagnosis (Parapsoriasis en Plaques? Mycosis Fungoides?).
Presented by DR. PAUL GROSS.

Mrs. S. K., a housewife aged 58, was referred by Dr. Alfred Lowenthal because of a generalized eruption of about six years' duration. The first lesion appeared on the breast; gradually other lesions developed. The condition was slightly itchy and worse in the summer, possibly owing to perspiration.

On the outer surface of both breasts are several reddish brown sharply circumscribed lesions of irregular outline, reaching the size of a palm. The skin is not infiltrated, and the epidermis appears wrinkled and atrophic. Some telangiectases are scattered throughout these lesions, and there is slight scaling. On the upper and lower extremities and the sides of the abdomen there are numerous patches about the size of a silver dollar. They are salmon pink and somewhat scaly. On the back are several distinctly yellowish irregularly shaped superficial patches. On the elbows, legs and thighs are a number of dark red lesions the size of a dime, suggestive of psoriasis. On the anterior surface of the left leg is an atrophic scar and at its border a brownish red flat nodule the size of a dime, infiltrating the deeper layer of the skin and surrounded by brownish pigmentation. This lesion is suggestive of a cutaneous nodule. Both forearms were treated with roentgen rays, 100 r on April 12 and on April 19, but failed to show improvement.

DISCUSSION

DR. PAUL GROSS: The lesions on the breasts show poikiloderma-like changes. On account of such changes some of the older dermatologists were inclined to

classify Brocq's disease as more closely related to idiopathic atrophy than to parapsoriasis. On the other hand, Dr. Harry Keil in a recent article (ARCH. DERMAT. & SYPH. **37**:465 [March] 1938) described these changes as strong evidence of incipient mycosis fungoides. I believe that it will be difficult in this case to make an early diagnosis of mycosis fungoides, since the lesions are superficial and a therapeutic test with fractional doses of roentgen rays had no effect. Another interesting feature is the presence on the lower extremities of some lesions that are almost typical of psoriasis.

DR. ARTHUR SAYER: I agree with everything that Dr. Gross has said about the clinical features of this case, but I cannot agree with his endorsement of Dr. Keil's views. I do not believe that Dr. Keil's conclusion should be accepted as final on the subject of the interrelationship of parapsoriasis, poikiloderma and mycosis fungoides. Dr. Keil has called attention to a rather interesting observation with which almost every one is familiar, and that is that cases in which a diagnosis of parapsoriasis or a similar condition has been reported in the literature by competent dermatologists subsequently proved to be instances of mycosis fungoides. I do not think that his conception, that in all cases parapsoriasis and poikiloderma will eventually prove to be mycosis fungoides, can be accepted at present. I have observed several cases of parapsoriasis for many years and still consider them such and not instances of mycosis fungoides.

DR. DAVID L. SATENSTEIN: This question interests me from another point of view: The members are all familiar with cases of this type in which a piece of tissue taken for histologic study failed to show definite characteristics. I think that the trouble lies with the staining methods employed. Silver and other stains to show the reticulum are necessary in cases in which one has to differentiate between psoriasis, parapsoriasis and mycosis fungoides clinically.

DR. MARION B. SULZBERGER: I agree entirely with Dr. Satenstein's remarks. What he said conforms to what J. Jadassohn told me many years ago, and I presented to him slides showing questionable mycosis fungoides. Professor Jadassohn stated that he could not decide whether these specimens showed early mycosis fungoides because the specimens were not impregnated to demonstrate the reticulum.

DR. ERICH URBACH, Vienna, Austria (by invitation): It is difficult to make a definite diagnosis in Dr. Gross's case. I recall a patient who for twenty-five years suffered from a similar cutaneous disease, which only at autopsy was demonstrated to be mycosis fungoides. Another point which I should like to stress is the resemblance of the lesions on the back, which are white and hard, to scleroderma.

DR. PAUL GROSS: With regard to the paper of Dr. Keil, its value lies in the careful review of the literature, in which he was able to demonstrate that in some of the original cases on which our conception of parapsoriasis en plaques had been built up the condition was later recognized as mycosis fungoides.

Folliculitis Decalvans et Atrophicans (Little), or Lichen Planus Acuminatus et Atrophicans (Feldman). Presented by DR. ADOLPH ROSTENBERG.

This patient, a Negress aged 50, presents an eruption of the scalp and body of twenty years' duration. The patient states that it followed laparotomy at the age of 30.

There is diffuse irregular alopecia over the entire scalp. The affected skin appears to be glossy, white and slightly atrophic. Throughout the scalp there are protruding follicles, filled with hard spinous plugs. Some of these are pierced by short broken-off hairs. In the parietal regions the alopecia is complete; here there are a large number of tiny brownish smooth dots, which appear to be the remains of atrophic hair follicles. On the abdomen there is a macular eruption which seems to be of the same character as that on the parietal region, except for

a few lesions which are definitely hard papules. On both elbows the eruption resembles lichen spinulosus.

The Wassermann test and other routine laboratory examinations gave negative results.

DISCUSSION

DR. SAMUEL FELDMAN: As I have repeatedly stated, E. G. G. Little admitted that the condition he described (*Brit. J. Dermat.* **27**:183, 1915) as folliculitis decalvans with lichen spinulosus is a variety of lichen planus. It may be labeled Little's disease if one chooses, but it is not folliculitis decalvans, because it has nothing to do with that disease. The pathologic picture of the disease in question consists of a dilated follicle with a horny plug, an increased granular layer and a sharply defined infiltration around the follicle. In this particular case the lesions on the head fit in well enough with lichen acuminatus et atrophicans. The lesions on the body, however, are not typical; one would expect large lesions with definite horny plugs and more pigmentation. I suggest a biopsy of the lesion of the body to corroborate the diagnosis and to differentiate the condition from ordinary lichen spinulosus.

DR. PAUL GROSS: This case seems to show the necessity in approaching this problem of considering the views expressed by the late L. K. McCafferty (ARCH. DERMAT. & SYPH. **19**:514 [Oct.] 1928). There is nothing in this case to suggest lichen planus.

DR. ADOLPH ROSTENBERG: This case still impresses me as a classic instance of what Little described as folliculitis decalvans, since the picture fits in well with Little's description.

Adenoma Sebaceum (Pringle Type), Associated with Recklinghausen's Disease. Presented by DR. LOUIS CHARGIN.

N. N., a clerk aged 33, single, presents a variety of lesions which first appeared about fifteen years ago and in the course of several years developed to the present extent. Around the nose and on the chin, just below the lip, there are lesions the size of a pinhead or a millet, densely set, reddish and somewhat soft to the touch. There is distinct seborrhea of the nasal region. There are numerous telangiectases. On the neck there are warty soft and pendulous lesions. On the right breast there is a soft pendulous tumor the size of an egg, and a similar, smaller one is present on the left side of the scrotum. Scattered over the trunk are pigmented spots. These are not as numerous nor as characteristic as usually seen in Recklinghausen's disease. There is no mental defect. The patient has a slight visual disturbance.

DISCUSSION

DR. ERICH URBACH, Vienna, Austria (by invitation): I know that the occurrence of the combination of Recklinghausen's and Pringle's disease has been recorded (Urbach, Erich, and Wiedmann, Albert: Morbus Pringle and Morbus Recklinghausen, *Arch. f. Dermat. u. Syph.* **158**:334-343, 1929). The cases were never investigated. About ten years ago I had a similar case, in which it was impossible to demonstrate clinical manifestations of both diseases but histologic studies with special stains showed the association of the two. I think that the two diseases have a similar background.

DR. PAUL GROSS: About eighteen years ago I studied a case of this type and could prove both diagnoses histologically. I have the photographs of a patient whom I saw a few years ago at Letchworth Village, New York, who, in addition to typical adenoma sebaceum (Pringle), had a large neurofibroma of the scalp. It is important to present these cases, because the combination of Pringle's disease with neurofibromatosis is not generally accepted.

A Case for Diagnosis (Pigmentation Following Treatment with Arsphenamine and Bismuth? Erythrose Péribuccale Pigmentaire de Brocq?). Presented by DR. SAMUEL FELDMAN.

M. S., a German housewife aged 42, came to the clinic of the Morrisania City Hospital because of hemiplegia on the right, which was diagnosed as cerebral thrombosis due to syphilis. After three months of antisyphilitic treatment the condition cleared for the most part, leaving a dilated and fixed right pupil and slight paralysis of the right side of the face. The treatment consisted of thirty-two injections of neoarsphenamine and thirty-six injections of bismuth subsalicylate and oral administration of potassium iodide. The total amount of neoarsphenamine injected was 12 Gm. About three months ago pigmentation appeared about the mouth. The patient has not used any cosmetics, such as freckle creams or hair dyes, containing silver preparations in any form.

There is a yellowish brown pigmentation with indistinct borders located about the mouth and chin. There is no evidence of pigmentation on the buccal mucous membrane or elsewhere on the body. The discoloration is considerably lighter under diascopic pressure, but it does not disappear entirely. It also varies in intensity from day to day. There is no erythema, scaling or other evidence of inflammation.

The Wassermann reaction of the blood and of the spinal fluid were negative; the colloidal gold curve was flat.

DISCUSSION

DR. LOUIS CHARGIN: Although I have by this time seen a considerable number of eruptions following administration of the arsphenamines, I do not recall a single case in which an arsphenamine eruption was limited to the skin of the lower jaw, nor have I encountered such pigmentation following the use of a bismuth preparation. The case impresses me as one of érythrose péribuccale pigmentaire. Dr. Feldman can, however, prove this diagnosis by trying to activate the lesions by administering arsphenamine or a bismuth preparation.

DR. GEORGE C. ANDREWS (by invitation): There is fine scaling on the patches. I have under observation a case of érythrose péribuccale pigmentaire now to which this case bears resemblance. That disease is interpreted as something akin to rosacea. In view of the scaling I suggest that an examination for fungi be made, to exclude monilia and tinea.

DR. ISIDORE M. LASHINSKY: While this picture may fit in with that of érythrose péribuccale pigmentaire, yet some of the features are lacking. The cases described by Brocq (*Presse méd.* **13**:627, 1923; *Bull. Soc. franç. de dermat. et syph.* **5**:339, 1927) and by G. Milian and A. Civatte (*Bull. Soc. franç. de dermat. et syph.* **8**:733, 1927) were mostly those of women suffering from syphilis. It is noteworthy that those authors suggested that the sympathetic nervous system is partly responsible for the condition. That is why the eruption becomes at times more flushed (érythrose). In this patient the pigmentation has remained unchanged for the last three months. In view of these points, one can accept the diagnosis of érythrose péribuccale pigmentaire with reservation.

DR. SAMUEL FELDMAN: I am inclined to agree with the opinion expressed by Dr. Chargin, that the pigmentation is probably not due to arsphenamine. It seems that when the patient is not flushed the lesions look brighter, and when he is flushed the color is darker. The pigmentation is not influenced by the arsphenamine, which the patient is still receiving. Therefore érythrose péribuccale pigmentaire is more likely than arsphenamine dermatitis.

A Case for Diagnosis (Epithelioma of the Lip? Ulcerative Tertiary Syphilis [?] on the Right Buccal Mucosa, with Lingual and Buccal Leukoplakia). Presented by DR. CHARLES PINES.

C. B., a man aged 62, presents a lesion on the lower lip which appeared about eight weeks ago. The patient thought it was a "cold sore" and kept irritating it

by picking and frequent application of iodine. He stated that he had had a gonorrheal infection thirty years ago but had not had syphilis.

Near the right angle of the mouth on the buccal mucosa there is a small round ulcer with a clean base. On the tongue and buccal mucosa near the corners of the mouth are many small whitish patches. On the right half of the lower lip is an irregular deep oval ulcer about 1.5 cm. in diameter, with a slightly necrotic base; this is partially covered by a bloody crust. The lesion is definitely indurated. There is no submental adenopathy. One small gland is palpable in the left anterior cervical triangle. The pharynx and tonsils are congested, and the uvula is edematous.

Dark field examination of material from the lesion on the lower lip gave negative results. The Wassermann reaction was 4 plus.

NOTE.—Subsequent histologic examination of a section taken from the lesion of the lip revealed typical squamous cell epithelioma.

DISCUSSION

DR. LOUIS CHARGIN: The lesion on the lower lip has existed for only the past eight weeks, and clinically it strongly suggests prickle cell epithelioma. This lesion is hard and indurated. The lesion on the cheek, however, is soft and clinically cannot be called epithelioma. With regard to treatment: In spite of the fact that I am inclined to diagnose epithelioma of the lower lip, I think antisyphilitic treatment for about fourteen days would not harm the patient. Perhaps even the lesion on the lower lip will prove to be a gumma after all.

DR. GEORGE C. ANDREWS (by invitation): I think a biopsy should be performed without further delay and that no antisyphilitic treatment should be tried.

DR. CHARLES PINES: I shall follow Dr. Chargin's suggestion and give the patient a few injections of a bismuth preparation. I do not think one can lose much by waiting to see if the lesion will respond to treatment.

Lupus Erythematosus of the Conjunctiva. Presented by DR. DAVID BLOOM.

F. C., a woman aged 36, has had an eruption on the face and scalp for the past eleven years. Below the eyes and on the bridge of the nose, in a butterfly formation, there are patches of erythema, scaling, telangiectasia and atrophy. The lower conjunctivas present marked redness and telangiectasia. In the occipital region of the scalp is an elongated plaque of alopecia with atrophy and telangiectasia, which at both sides extends upward to the region behind the ears. On both sides of the neck is a chain of hard glands varying in size from that of an almond to that of a walnut which, according to the patient's statement, has been present for ten years.

Roentgenograms of the lungs did not reveal any abnormality. The blood and the differential count were normal. The Wassermann reaction was negative, and the basal metabolic rate was within normal limits.

The patient has received many injections of sodium gold thiosulfate and of bismuth subsalicylate intramuscularly; some improvement has resulted. Sulfanilamide was administered without benefit.

DISCUSSION

DR. CHARLES LERNER: In my opinion, scarring of the cutaneous surface of the lid caused ectropion and this produced conjunctivitis. I do not think that the conjunctiva is directly affected by lupus erythematosus.

DR. PAUL GROSS: I have under my care a patient who has typical lupus erythematosus of the face and conjunctiva and in whom the lesion of the eye is confined to the inner canthus and conjunctiva, without involvement of the outer part of the lid. It is important that these patients wear dark glasses.

DR. SAMUEL FELDMAN: Patients with lupus erythematosus are sensitive to light, and I do not think they should be given sulfanilamide, which is known to be a strong photosensitizing agent.

DR. DAVID BLOOM: Lupus erythematosus of the conjunctiva is rarely observed and warrants recording.

Recklinghausen's Disease with Nevi, Deformity of Bone and Tumefaction of Soft Tissue. Presented by DR. CHARLES LERNER.

S. R., a youth aged 17, was previously presented before this society in March 1934 with 3 other members of his family (ARCH. DERMAT. & SYPH. **30**:743 [Nov.] 1934).

Since that time an enlargement of the neck has developed. On first impression it appeared that the growth was a bony tumor similar to that of his maternal uncle, who had a large bony tumor removed from the tibia. However, a roentgenogram of the neck showed marked deformity of the midcervical vertebrae and right lateral deviation, as well as marked kyphosis at the point of greatest angulation. The body of what appeared to be the fourth cervical vertebra was in anterior luxation in relation to the body of the fifth, resulting in an angulation of over 45 degrees. The distortion and development of the bodies of the vertebrae of the middle and the upper part of the cervical area appeared ascribable to a congenital anomaly and to faulty epiphysial development.

There was pressure atrophy backed by zones of condensation at the points of pressure. The body of the sixth cervical vertebra showed increased porosity, probably the result of expansion of the haversian spaces, and there was considerable thickening of the soft tissues in the upper part of the cervical area; this, however, appeared independent of the spinal deformity.

There was rotation, with considerable right lateral deviation, of the upper dorsal portion of the spine, this again being of long standing, as suggested by the narrowing of the bodies of the vertebrae on the concave side of the deformity.

Supernumerary ribs were developing from the bodies and transverse processes of the seventh cervical vertebra.

In a further study of the thorax a diminished illumination in the apical area appeared due to the spinal deformity and to tumefaction of soft tissue. This, however, appeared to be a continuation of the infiltration of soft tissue a short distance into the subclavicular space on the right side.

There was a thoracic deformity due to asymmetric development of the ribs, mainly on the right side.

The total cardiac area was relatively small, with the transverse diameter about 3 cm. below average normal; it was otherwise of normal contour.

There was moderate lymphoid nodulation at the hilus, with slight secondary thickening of the root branches. The peripheral pulmonary fields were otherwise clear, with no evidence of recent parenchymatous infiltration or pleural involvement.

A diagnosis of marked deformity of the cervical spine, probably ascribable in the main to congenital faulty epiphysial development, tumefaction of soft tissue in the cervical area and asymmetry in thoracic development, with supernumerary cervical ribs, was made.

Dermatitis Herpetiformis. Presented by DR. ARTHUR SAYER.

K. C., a white woman aged 58, single, has been suffering from a pruritic eruption for four years. She has had periods of complete remission. There has been no ingestion of drugs. Menstruation ceased about ten years ago; the menopause was free of symptoms. The Wassermann test, urinalysis and a complete examination of the blood gave negative results.

She has a diffuse erythematous papular and papulovesicular eruption, mainly localized on the upper part of the back and the buttocks. The lesions range in

size from that of a pinhead to that of a split pea. There is marked grouping. Numerous whitish superficial scars are scattered over the rest of the back, the sites of former lesions. There is a sparser similar eruption on the arms, forearms, thighs, legs and scalp.

Dermatitis Herpetiformis. Presented by DR. MAX B. KAMPF.

W. C., aged 53, presents an eruption of four years' duration. At first it was limited to the buttocks, but it soon spread to the extremities. Since its beginning there have been short periods of remission. The patient insists that the lesions never appeared on the trunk but always on the upper and lower extremities. The eruption consists of papules, vesicles and small bullae, occurring in groups on an erythematous base; some lesions are crusted. The lesions are confined to the upper and lower extremities, although there is some evidence of eruption on both ears and neck. The bullae are turbid, and some are hemorrhagic.

DISCUSSION OF TWO CASES OF DERMATITIS HERPETIFORMIS

DR. SAMUEL M. PECK: I had unusual results in 2 cases of Duhring's disease, one of which was reported in the *Archives of Dermatology and Syphilology* several years ago. The case was also observed by many dermatologists throughout the country, who concurred in the diagnosis. Both patients were men, the first in his twenties and the second in his late thirties, having had Duhring's disease for years. The diagnosis was made by the elder Jadassohn, who had treated him for many years. Both patients had a basal metabolic rate between —22 and —24 per cent. Both were unusually sensitive to staphylococcus toxoid (Lederle). The ingestion of thyroid and the injection of small doses of staphylococcus toxoid completely cleared the lesions in both cases. The first patient has been free of lesions for about a year; the second has been clear for several months now. In both cases there is a tendency to recurrence if thyroid medication is stopped. The injections of staphylococcus toxoid also must be kept up. It was of interest to note that when the latter substance was given in too large a dose, new lesions tended to develop.

DR. ERICH URBACH, Vienna, Austria (by invitation): In the past three years I have investigated every case of bullous dermatosis at my clinic. On the basis of a positive reaction to a cutaneous test with iodides alone one cannot make a diagnosis of dermatitis herpetiformis. I have seen conditions resembling dermatitis herpetiformis which eventually were shown to be reactions to a focus of infection. The removal of infected tonsils or teeth cleared up the eruption. I have with me photographs made in 3 such cases. It is difficult to arrive at a definite decision in these cases, even with much material to study.

DR. ARTHUR SAYER: I want to call attention to the presence of lesions on the scalp, which I think is rather unusual in Duhring's disease. The basal metabolic tests which Dr. Peck reported are not conclusive, because the normal figures run from +15 to —15. A figure of —18 should be checked, because it is close to normal.

Granuloma Annulare. Presented by DR. ADOLPH ROSTENBERG.

Erythema Nodosum. Presented by DR. MARION B. SULZBERGER.

Lichen Planus with Lesions on the Palms and Soles. Presented by DR. LOUIS CHARGIN.

Book Reviews

Chaulmoograöl. By Hans Schlossberger. Pp. 140. Berlin: Julius Springer, 1938.

Among the few chemical preparations which have a curative effect in leprosy, first place is taken by oils obtained from the seeds of different members of the plant family of Flacourtiaceae, particularly by chaulmoogra oil, and certain preparations obtained from those oils, the effective components of which are apparently the characteristic unsaturated fatty acids. These oils have apparently a specific influence on the disease process. The importance of chaulmoogra oil in the treatment of leprosy justifies fully the writing of a monograph on this subject. Professor Schlossberger, of the Robert Koch Institute in Berlin, Germany has performed a meritorious piece of work in writing this monograph. He believes that although the treatment is only partly satisfactory, the way of improving it is by correlation of clinical and laboratory investigation. The monograph contains the history of the use of the oils in the treatment of leprosy, which dates back many hundreds of years and is cited in the medical works of India and China. The names of the different flacourtiaceae from which chaulmoogra oil and related vegetable fats are obtained are enumerated. Some of the subjects thoroughly discussed are: chemistry, synthetic preparations, pharmacology, toxicology, effect on different animals, lethal doses for different animals, absorption, distribution in the body, elimination and the effect on different organs. Together with an enormous bibliography, these make up a complete monograph.

Directory of Dermatologic Societies *

INTERNATIONAL

Tenth International Congress of Dermatology and Syphilology

Oliver S. Ormsby, President, 25 E. Washington St., Chicago.
Paul A. O'Leary, Secretary-General, 102–2nd Ave., S. W., Rochester, Minn.
Place: New York. Time: Summer 1940.

Pan American Medical Association, Section of Dermatology and Syphilology

Elmore B. Tauber, President, 19 W. 7th St., Cincinnati.
Austin W. Cheever, Secretary, 49 Bay State Rd., Boston.

FOREIGN

British Association of Dermatology and Syphilology (Canadian Branch)

Harold Orr, President, 10189 101st St., Edmonton.
Don Mitchell, Secretary-Treasurer, 1414 Drummond St., Montreal.

Royal Society of Medicine, Section of Dermatology

H. W. Barber, President, 7 Devonshire Pl., London, W. 1.
Louis Forman, Secretary, 7 Devonshire Pl., London, W. 1.

NATIONAL

American Medical Association, Scientific Assembly, Section on Dermatology and Syphilology

J. Bedford Shelmire, Chairman, 1719 Pacific Ave., Dallas, Texas.
C. F. Lehmann, Secretary, 705 E. Houston St., San Antonio, Texas.
Place: St. Louis. Time: May 15-19, 1939.

American Academy of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
Earl D. Osborne, Secretary, 471 Delaware Ave., Buffalo, N. Y.
Place: St. Louis. Time: November 1938.

American Board of Dermatology and Syphilology

Howard Fox, President, 140 E. 54th St., New York.
C. Guy Lane, Secretary-Treasurer, 416 Marlborough St., Boston.
Place: St. Louis. Time: Nov. 11-12, 1938.

American Dermatological Association

Francis E. Senear, President, 55 E. Washington St., Chicago.
Fred D. Weidman, Secretary, University of Pennsylvania, Philadelphia.
Place: Seigniory Club, Montebello, Ontario, Canada. Time: May 1939.

Society for Investigative Dermatology

George M. MacKee, President, 200 W. 59th St., New York.
S. M. Becker, Secretary, University of Chicago, Department of Medicine, Chicago.

* Secretaries of dermatologic societies are requested to furnish the information necessary for the editor to make this list complete and to keep it up to date.

SECTIONAL

Central States Dermatological Association

George H. Belote, President, University Hospital, Ann Arbor, Mich.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.

Mississippi Valley Dermatological Society

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.

New England Dermatological Society

Fred S. Burns, President, 83 Marlborough St., Boston.
B. Appel, Secretary, 483 Beacon St., Boston.

Northern New Jersey Dermatological Society

Francis McCauley, President, 31 Lincoln Pk., Newark.
Henri Abel, Secretary, 339 Union Ave., Elizabeth, N. J.
Place: Academy of Medicine of Northern New Jersey, Newark. Time: Third Tuesday of March, April, October and December.

Southeastern Dermatological Association

J. L. Kirby-Smith, Chairman, 204 Laura St., Jacksonville, Fla.
Joseph A. Elliott, Secretary, Professional Bldg., Charlotte, N. C.

Southern Medical Association, Section on Dermatology and Syphilology

M. Toulmin Gaines, Chairman, 404 Merchants National Bank Bldg., Mobile, Ala.
Clinton W. Lane, Secretary, 508 N. Grand Ave., St. Louis, Mo.

STATE

California Medical Association, Scientific Assembly, Dermatology and Syphilology Section

Norman N. Epstein, Chairman, 450 Sutter St., San Francisco.
Arne E. Ingels, Secretary, 490 Post St., San Francisco.

Connecticut State Medical Society, Section on Dermatology

James D. Gold, Chairman, 839 Myrtle Ave., Bridgeport.
Albert Levenson, Secretary, 881 Lafayette St., Bridgeport.

Florida Society of Dermatology and Syphilology

C. A. Andrews, Chairman, 706 Franklin St., Tampa.
Lauren Sompayrac, Secretary, 204 Laura St., Jacksonville.

Louisiana Dermatological Society

M. T. Van Studdiford, President, 912 Pere Marquette Bldg., New Orleans.
R. A. Oriol, Secretary-Treasurer, 921 Canal St., New Orleans.

Massachusetts Medical Society, Section on Dermatology and Syphilology

George A. Dix, President, 6 Ashland St., Worcester.
J. Harper Blaisdell, Secretary, 45 Bay State Rd., Boston.

Medical Society of the State of New York, Section on Dermatology and Syphilology

Mark Heiman, Chairman, 600 Medical Arts Bldg., Syracuse.
Timothy J. Riordan, Secretary, 136 E. 64th St., New York.

MEDICAL SOCIETY OF THE STATE OF PENNSYLVANIA
SECTION ON DERMATOLOGY

L. G. Beinhauer, Chairman, 5026 Jenkins Arcade Bldg., Pittsburgh.
V. C. Garner, Secretary, Germantown Professional Bldg., Philadelphia.
Place: Scranton. Time: October 1938.

MICHIGAN STATE MEDICAL SOCIETY, SECTION ON DERMATOLOGY AND SYPHILOLOGY

Ruth Herrick, Chairman, 26 Sheldon Ave., S. E., Grand Rapids.
Eugene A. Hand, Secretary, 801 Second National Bank Bldg., Saginaw.

MINNESOTA DERMATOLOGICAL SOCIETY

L. A. Brunsting, President, 102–2d Ave., S. W., Rochester.
F. W. Lynch, Secretary-Treasurer, Lowry Medical Arts Bldg., St. Paul.
Time: First Friday in October, December, February and April.

OKLAHOMA STATE DERMATOLOGICAL SOCIETY

Onis George Hazel, President, Osler Bldg., Oklahoma City.
Everett S. Lain, Secretary, Medical Arts Bldg., Oklahoma City.

TEXAS DERMATOLOGICAL SOCIETY

Everett R. Seale, President, 1215 Walker Ave., Houston.
Duncan O. Poth, Secretary, 414 Navarro St., San Antonio.

LOCAL

BALTIMORE-WASHINGTON DERMATOLOGICAL SOCIETY

Herman E. Kittredge, President, 1835 I St., N. W., Washington, D. C.
I. Louis Sandler, Secretary, 1835 I St., N. W., Washington, D. C.
Place: Alternate cities. Time: Third Thursday of each month.

BRONX DERMATOLOGICAL SOCIETY

Samuel M. Peck, President, 125 E. 72d St., New York.
Henry Silver, Secretary, 290 West End Ave., New York.

BROOKLYN DERMATOLOGICAL SOCIETY

David L. Satenstein, President, 57 W. 57th St., New York.
M. Edward Goebel, Secretary, 842 Union St., Brooklyn.
Time: Third Monday of each month except June, July, August and September.

BUFFALO-ROCHESTER DERMATOLOGICAL SOCIETY

Clarence H. Peachey, President, 197 S. Goodman St., Rochester, N. Y.
Richard L. Saunders, Secretary, 333 Linwood Ave., Buffalo.

CENTRAL NEW YORK DERMATOLOGICAL SOCIETY

Rudolph Ruedemann Jr., President, 256 State St., Albany.
Harry D. Parkhurst, Secretary-Treasurer, 264 Genesee St., Utica, N. Y.

CHICAGO DERMATOLOGICAL SOCIETY

Hamilton Montgomery, President, Mayo Clinic, Rochester, Minn.
Herbert Rattner, Secretary, 25 E. Washington St., Chicago.
Place: Chicago. Time: Third Wednesday in January 1938.

CINCINNATI DERMATOLOGICAL SOCIETY

Leon Goldman, President, Doctors Bldg., Cincinnati.
George E. Clarke, Secretary-Treasurer, 19 W. 7th St., Cincinnati.
Place: Cincinnati. Time: First Wednesday of each month, except June, July, August and September.

CLEVELAND DERMATOLOGICAL SOCIETY

John Gammel, President, 1020 Huron Rd., Cleveland.
Charles G. La Rocco, Secretary, 2060 E. 9th St., Cleveland.

DETROIT DERMATOLOGICAL SOCIETY

G. Warren Hyde, President, 2501 W. Grand Blvd., Detroit.
Thomas H. Miller, Secretary-Treasurer, 1305 David Whitney Bldg., Detroit.
Place: Detroit. Time: May 1939.

LOS ANGELES DERMATOLOGICAL SOCIETY

Thomas W. Nisbet, President, 65 N. Madison Ave., Pasadena, Calif.
C. R. Caskey, Secretary, 1930 Wilshire Blvd., Los Angeles.
Time: Second Tuesday of each month, October to May, inclusive.

MANHATTAN DERMATOLOGIC SOCIETY

Max Scheer, Chairman, 509 Madison Ave., New York.
Anthony C. Cipollaro, Secretary, 40 E. 61st St., New York.

MONTREAL DERMATOLOGICAL SOCIETY

B. Usher, President, 1538 Sherbrooke St., W., Montreal, Canada.
Paul Poirier, Secretary, 450 Sherbrooke St., E., Montreal, Canada.

NEW YORK ACADEMY OF MEDICINE, SECTION OF DERMATOLOGY AND SYPHILIS

Eugene F. Traub, Chairman, 140 E. 54th St., New York.
Louis Tulipan, Secretary, 224 E. 17th St., New York.

NEW YORK DERMATOLOGICAL SOCIETY

J. Frank Fraser, President, 100 W. 59th St., New York.
Frank C. Combes, Secretary, 80 W. 40th St., New York.

OMAHA DERMATOLOGICAL SOCIETY

Donald J. Wilson, President, 1113 Medical Arts Bldg., Omaha.
Leonard J. Owen, Secretary-Treasurer, 954 Stuart Bldg., Lincoln.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Thomas Butterworth, Chairman, 411 Walnut St., Reading, Pa.
Herman Beerman, Secretary, 255 S. 17th St., Philadelphia.
Time: Third Friday of each month from September to May, inclusive.

PITTSBURGH DERMATOLOGICAL SOCIETY

John C. Kerr, President, 62 14th St., Wheeling, W. Va.
Marvin B. Goldstein, Secretary, Stambaugh Bldg., Youngstown, Ohio.

ST. LOUIS DERMATOLOGICAL SOCIETY

A. H. Conrad, President, 3720 Washington Blvd., St. Louis.
Roy L. Kile, Secretary-Treasurer, 3720 Washington Blvd., St. Louis.
Place: Barnard Free Skin and Cancer Hospital. Time: 2 p. m., second Wednesday of each month.

SAN FRANCISCO DERMATOLOGICAL SOCIETY

Norman Epstein, President, 450 Sutter St., San Francisco.
H. V. Allington, Secretary, 3115 Webster St., Oakland.
Place: San Francisco. Time: Third Friday of November 1937.